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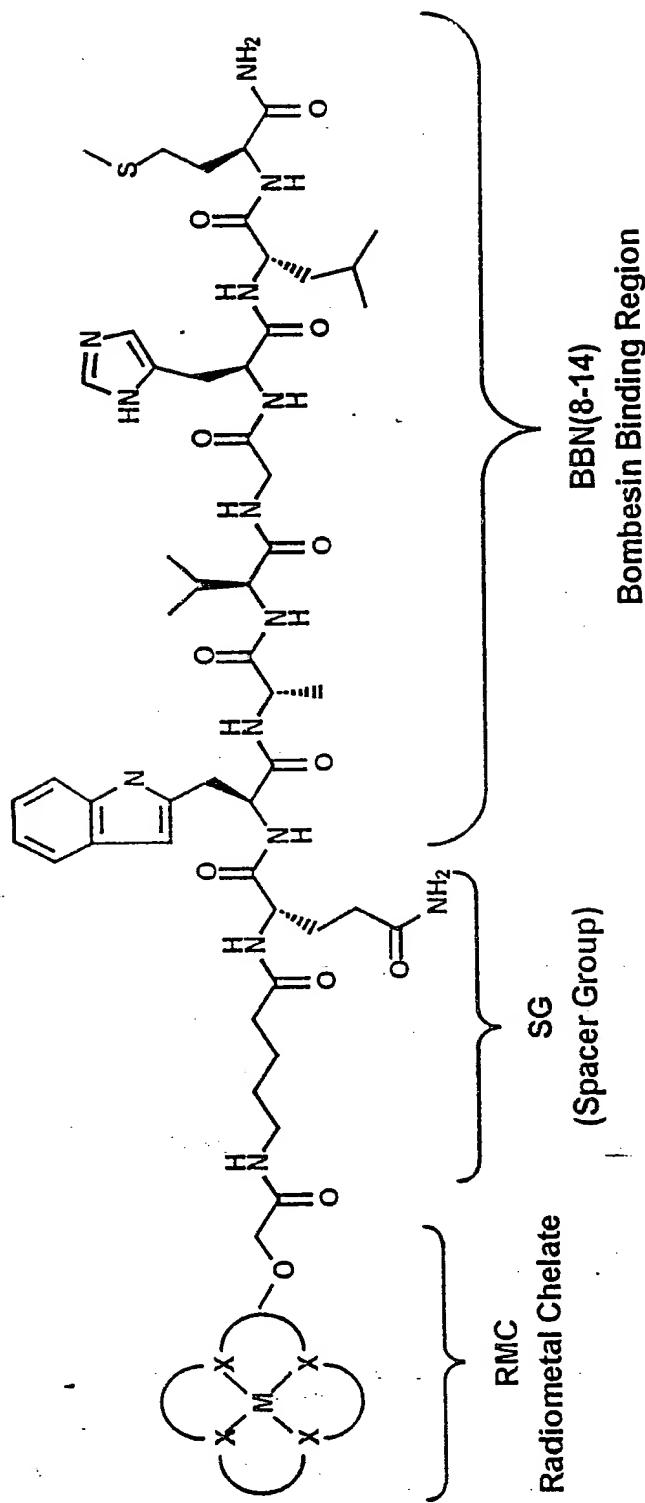
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SCANNED # 14

Radiometal Conjugate

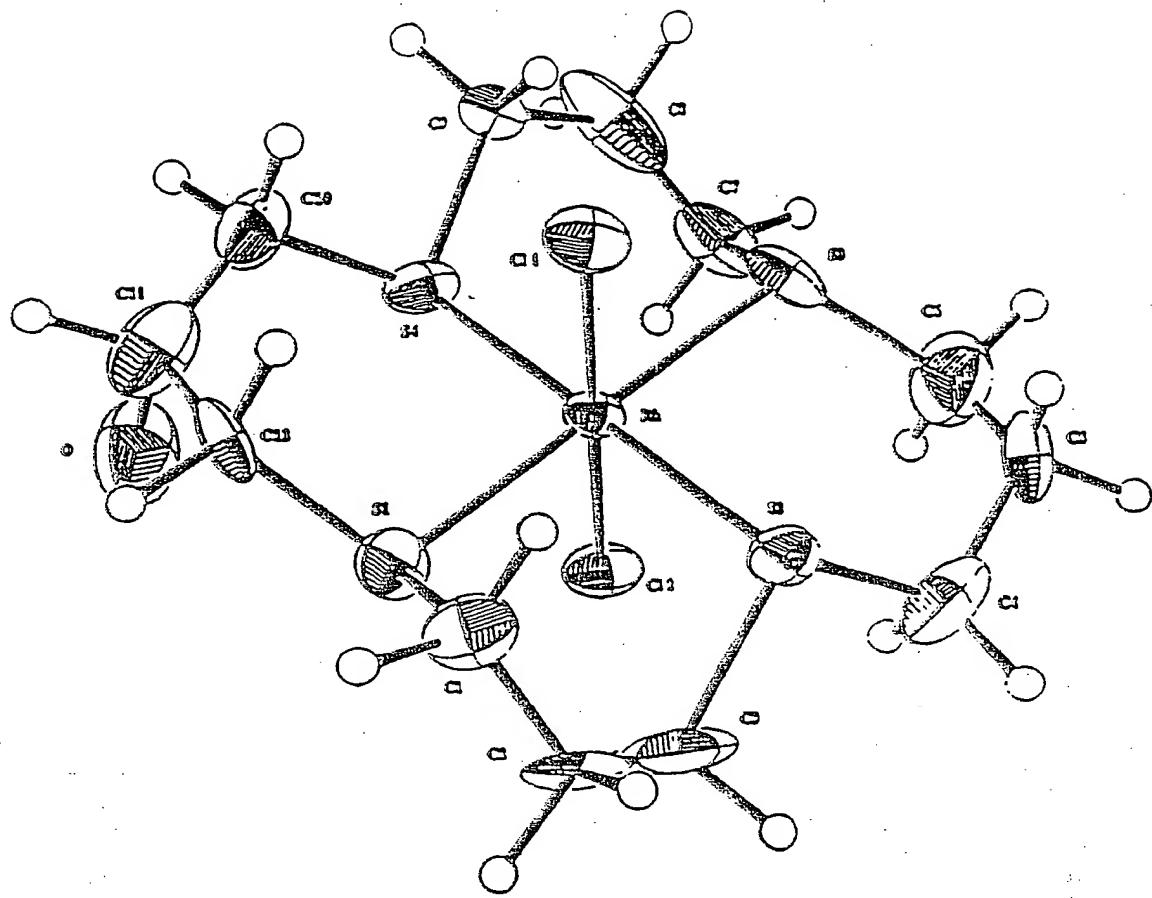


Radiometal conjugate of a BBN analogue that has high affinity for GRP receptors.

RMC=Radiometal chelate, where M=^{99m}Tc, ^{186/188}Re, ¹⁰⁵Rh and X=chelating atoms.

SG=Spacer group or linker that covalently attaches the chelate to the N-terminal end of the BBN binding region (BBN_{BR})

Figure 1



ORTEP Drawing of $\{\text{Rh}[16]\text{aneS}_4\text{-Cl}_2\}^+$

Figure 2

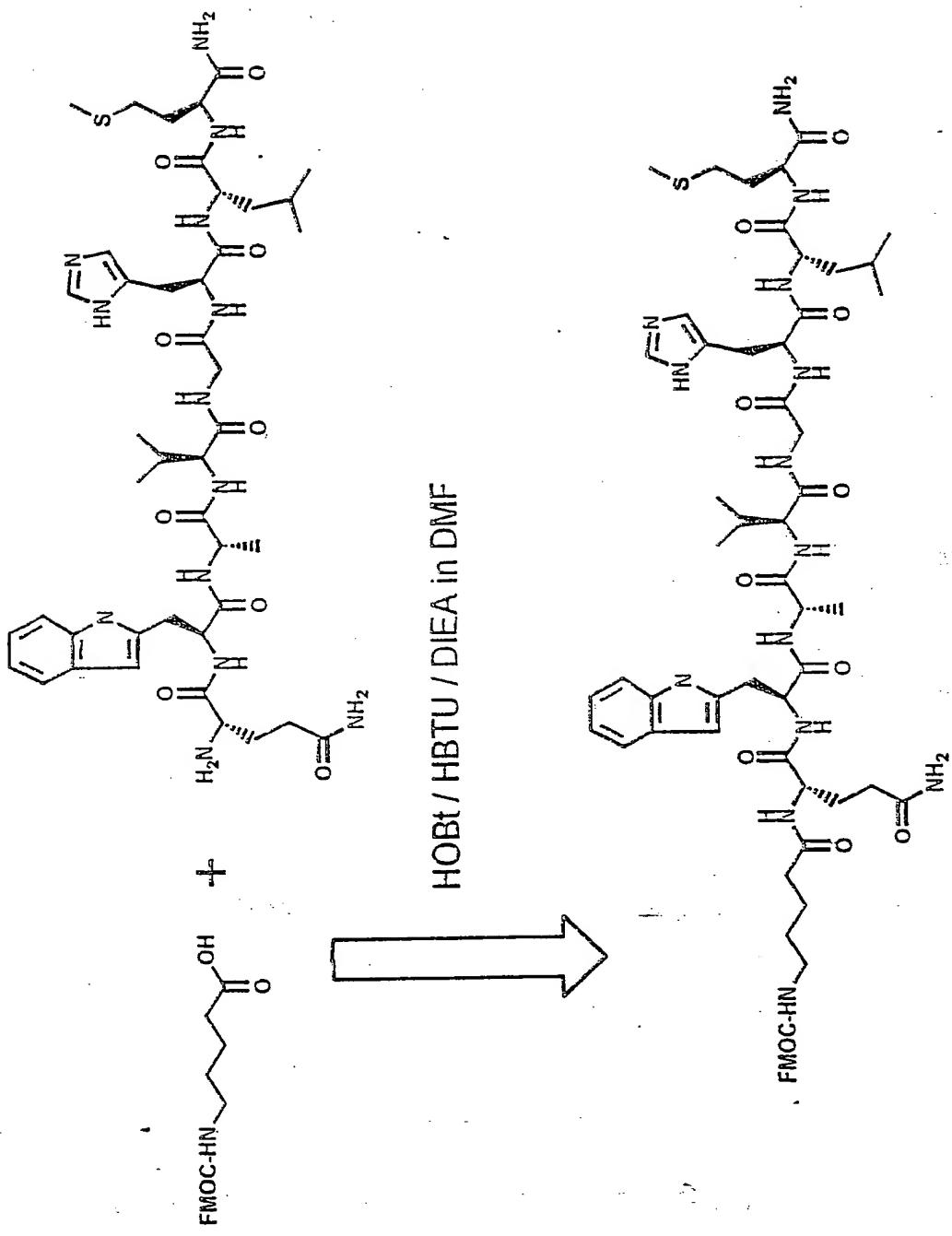


Figure 3

HOBT / HBTU / DIEA in DMF

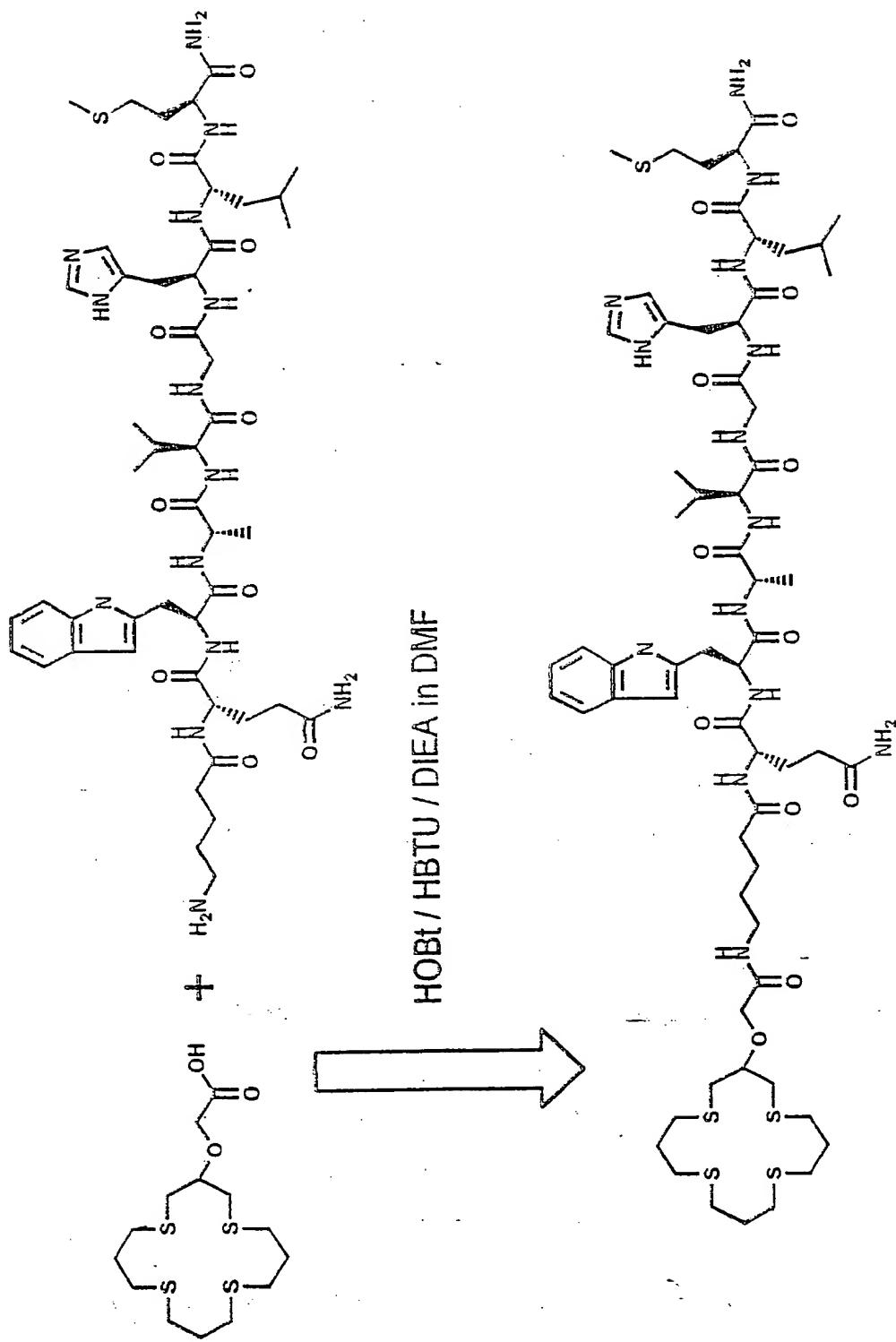


Figure 4

mlP-Lys³-BOMBESIN
Iodinated Bombesin Analogues

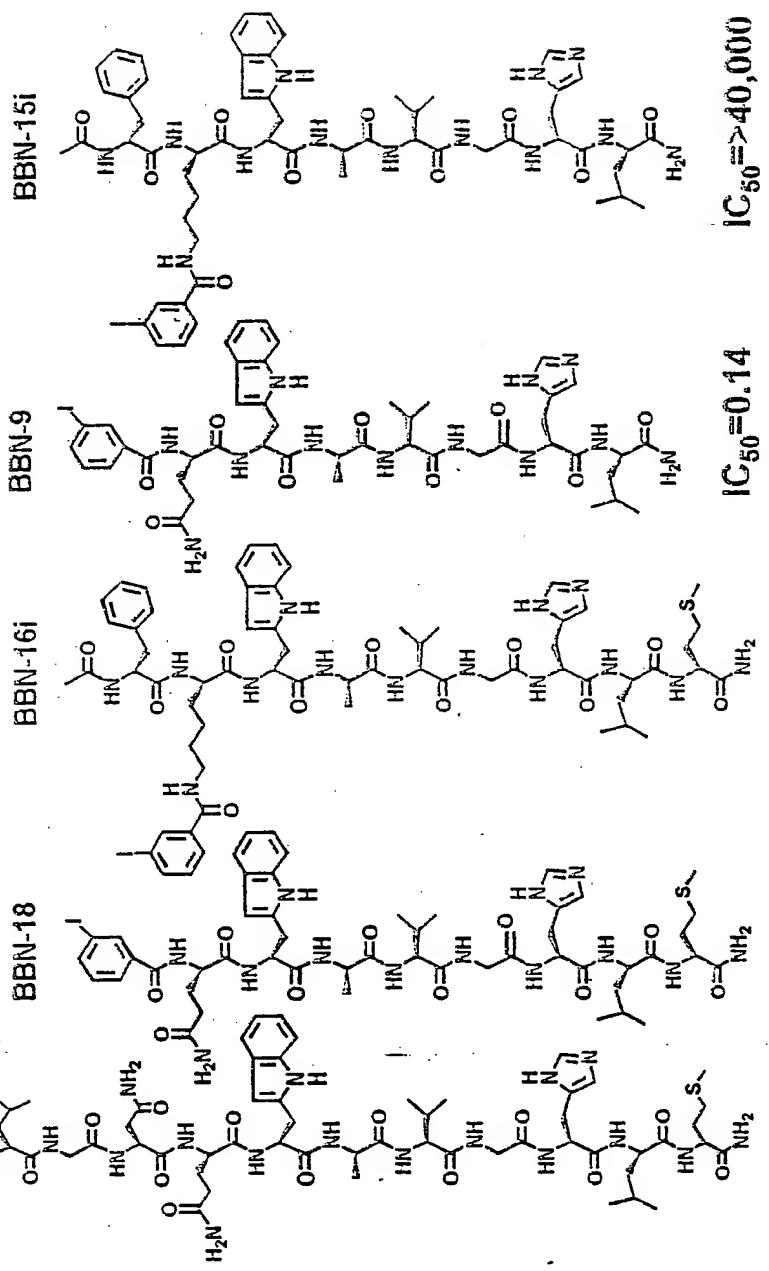


Figure 5

Tethered Bombesin Analogues

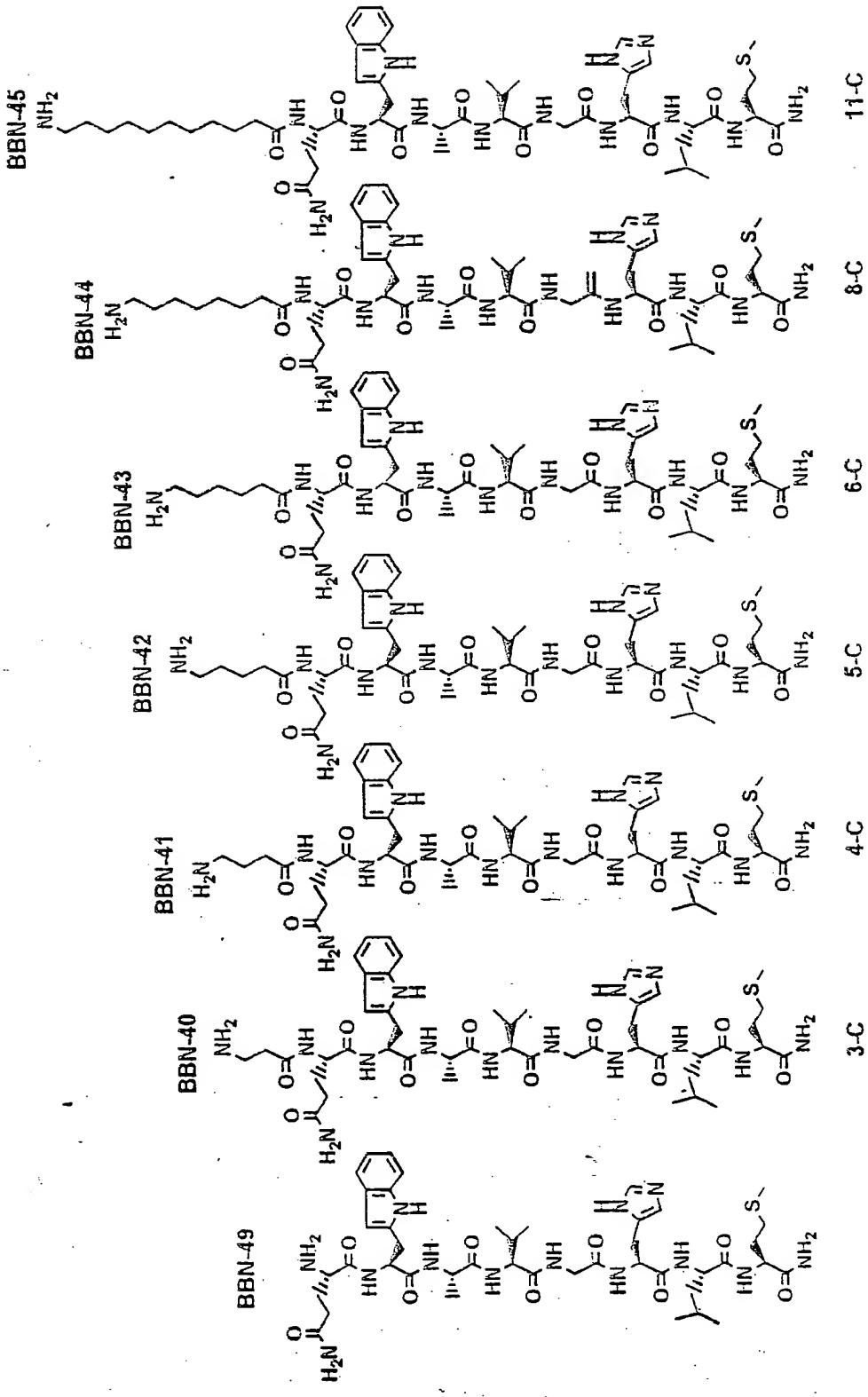
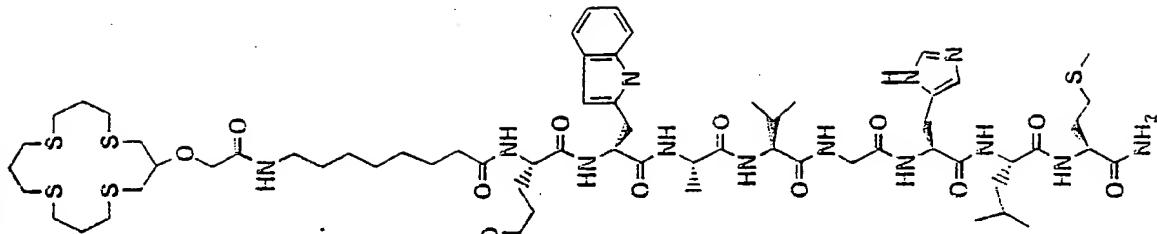


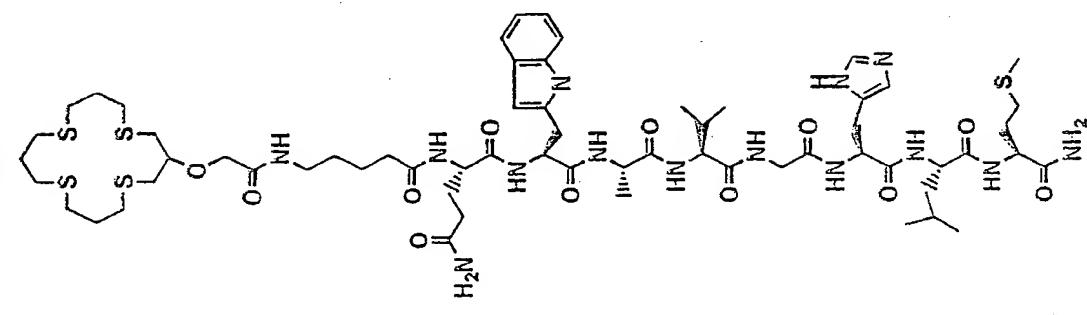
Figure 6

[16]aneS₄ Bombezin Analogues

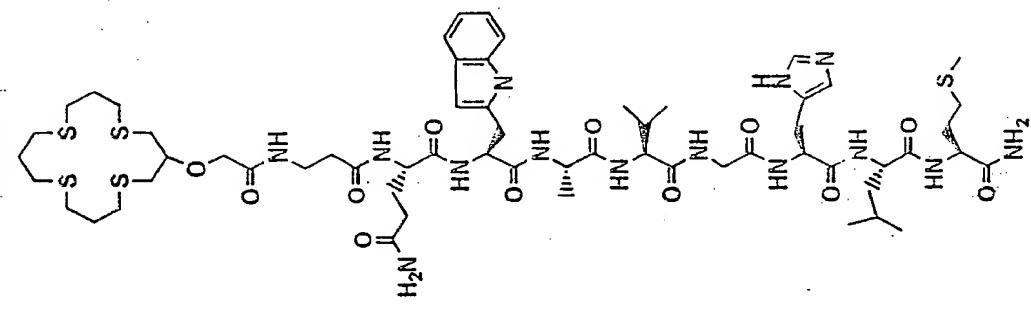
BBN-47



BBN-37



BBN-46



BBN-22

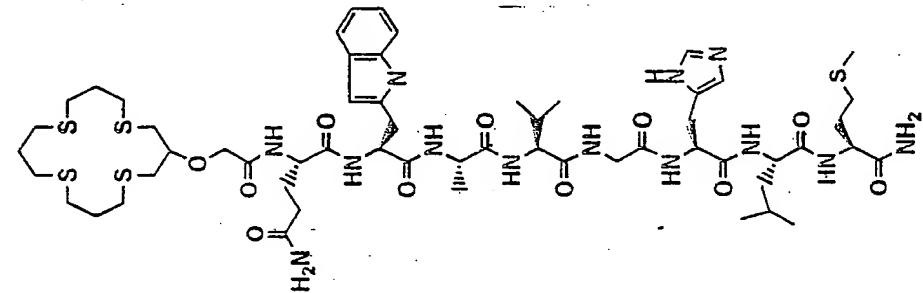


Figure 7

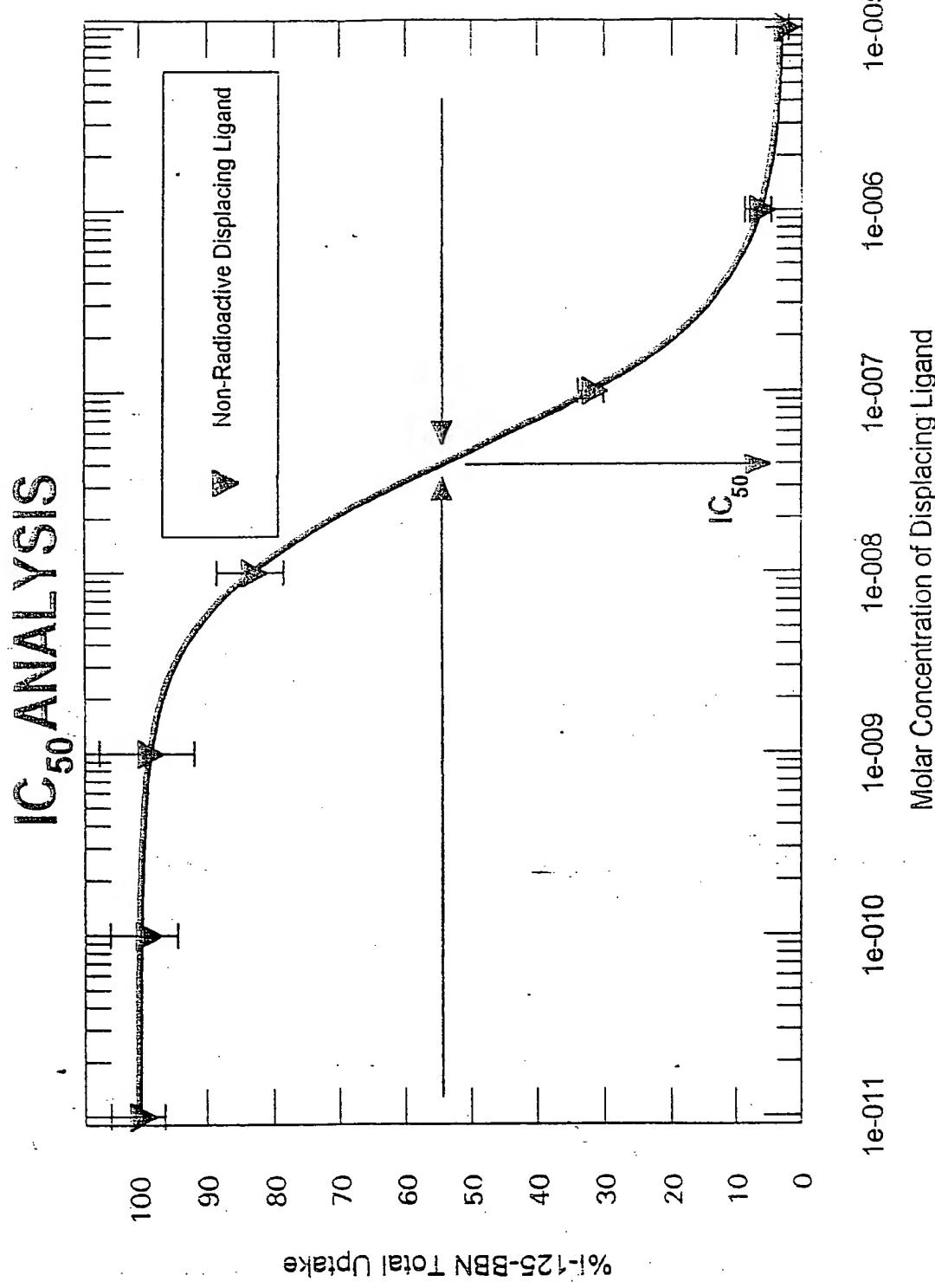


Figure 8

Rhodium-[16]aneS₄ Bombesin Analogues

BBN-47

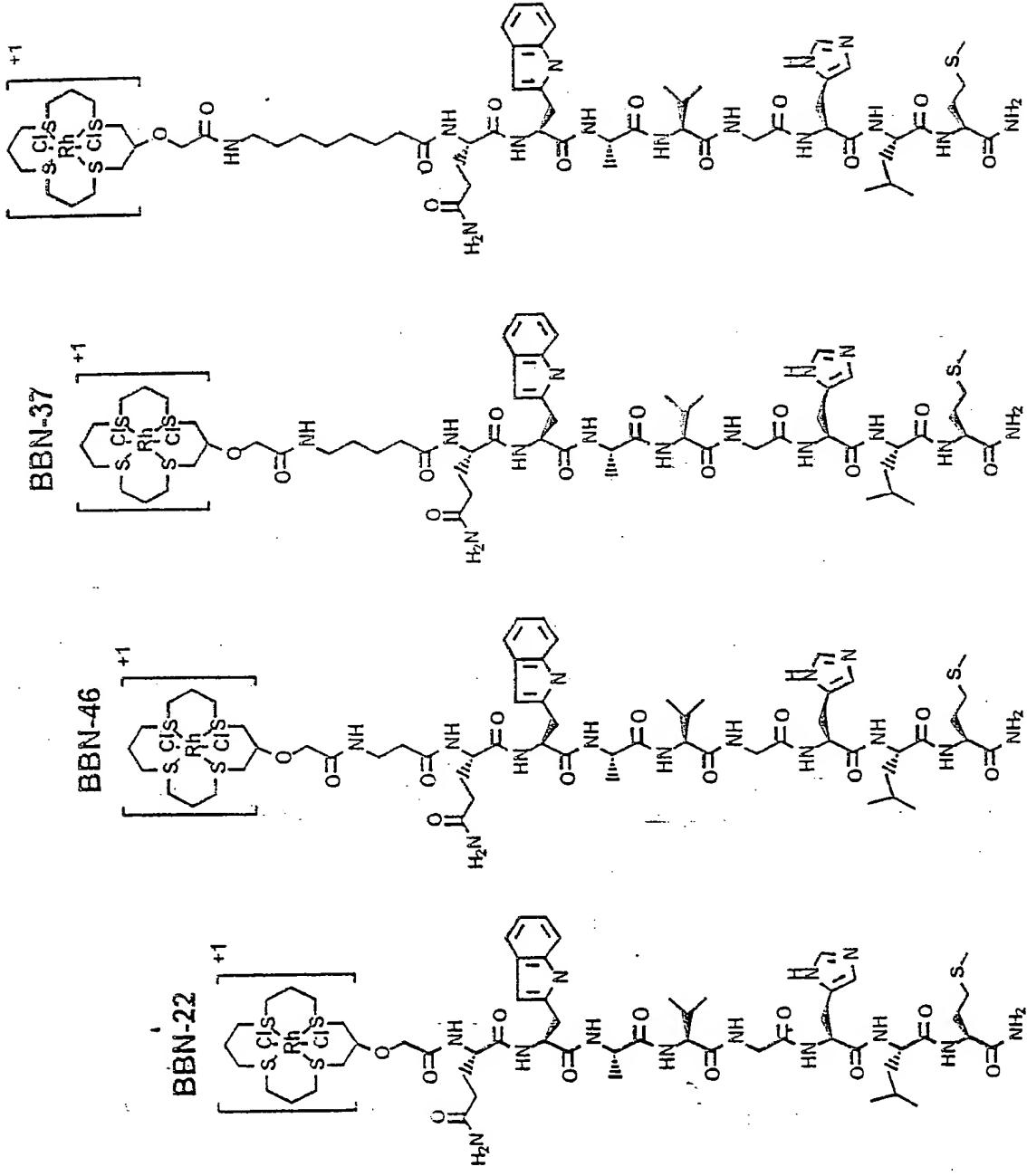
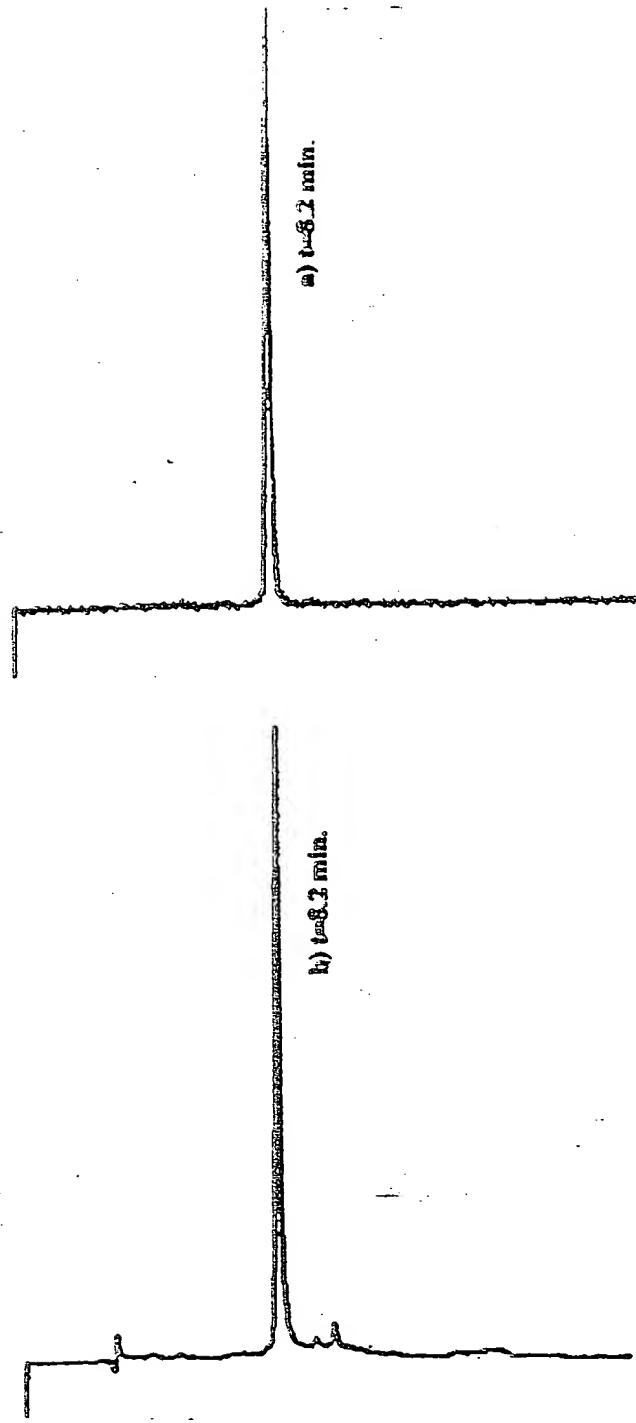


Figure 9

A.



HPLC Chromatogram of Rhodium-85-37
Top: $^{105}\text{RhCl}_2\text{-BBN-37}$
Bottom: $\text{RhCl}_2\text{-BBN-37}$

Figure 10

^{125}I -Tyr⁴-Bombesin Internalization
Efflux in ^{125}I -Tyr⁴-BBN Free Buffer

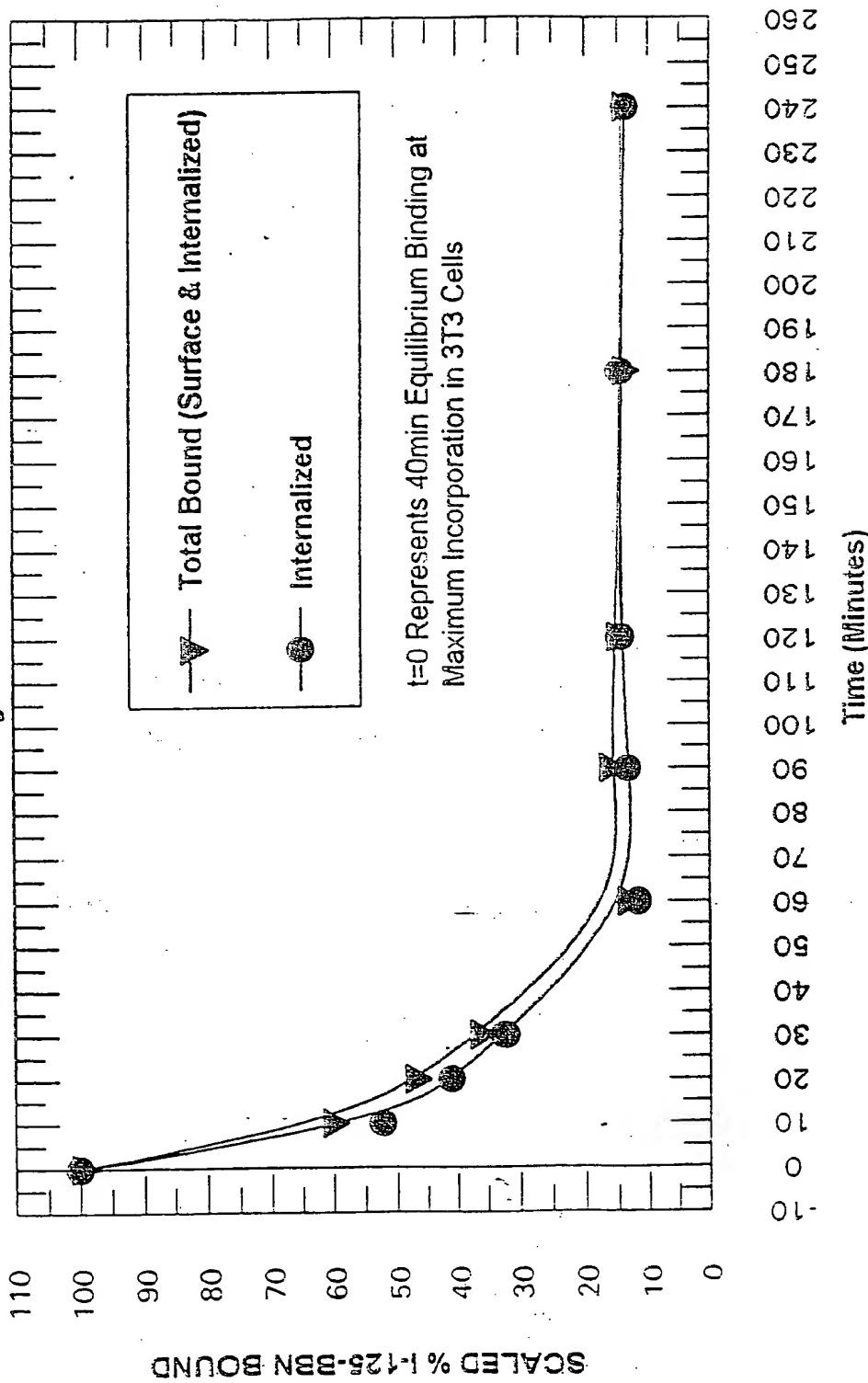


Figure 11

125 I-Bombesin Internalization

Efflux in 125 I-Free Buffer

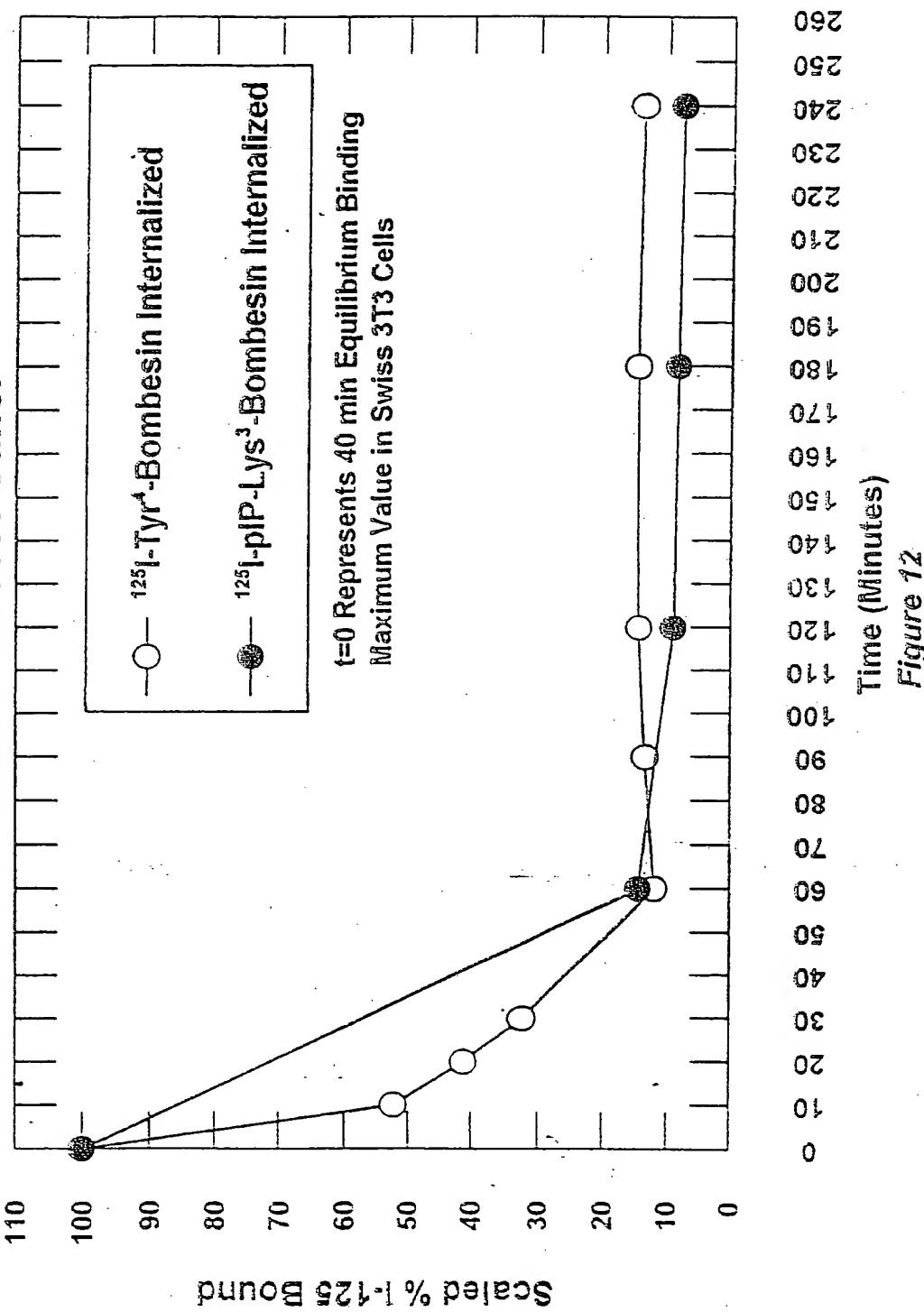


Figure 12

Efflux of ^{105}Rh -BBN-37 in Swiss 3T3 Cells (Normalized Data)

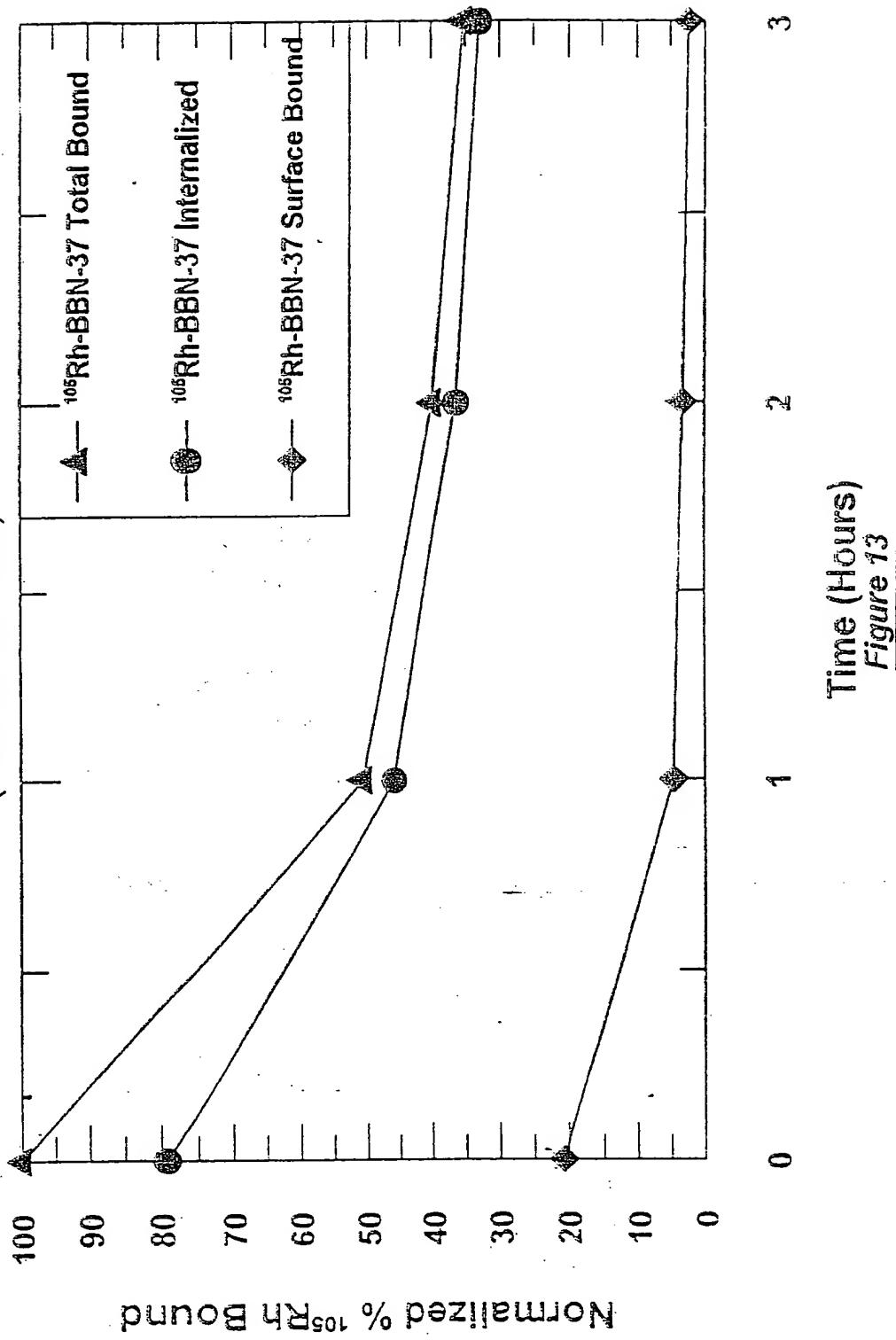


Figure 13

¹⁰⁵Rhodium Bombesin Analogues

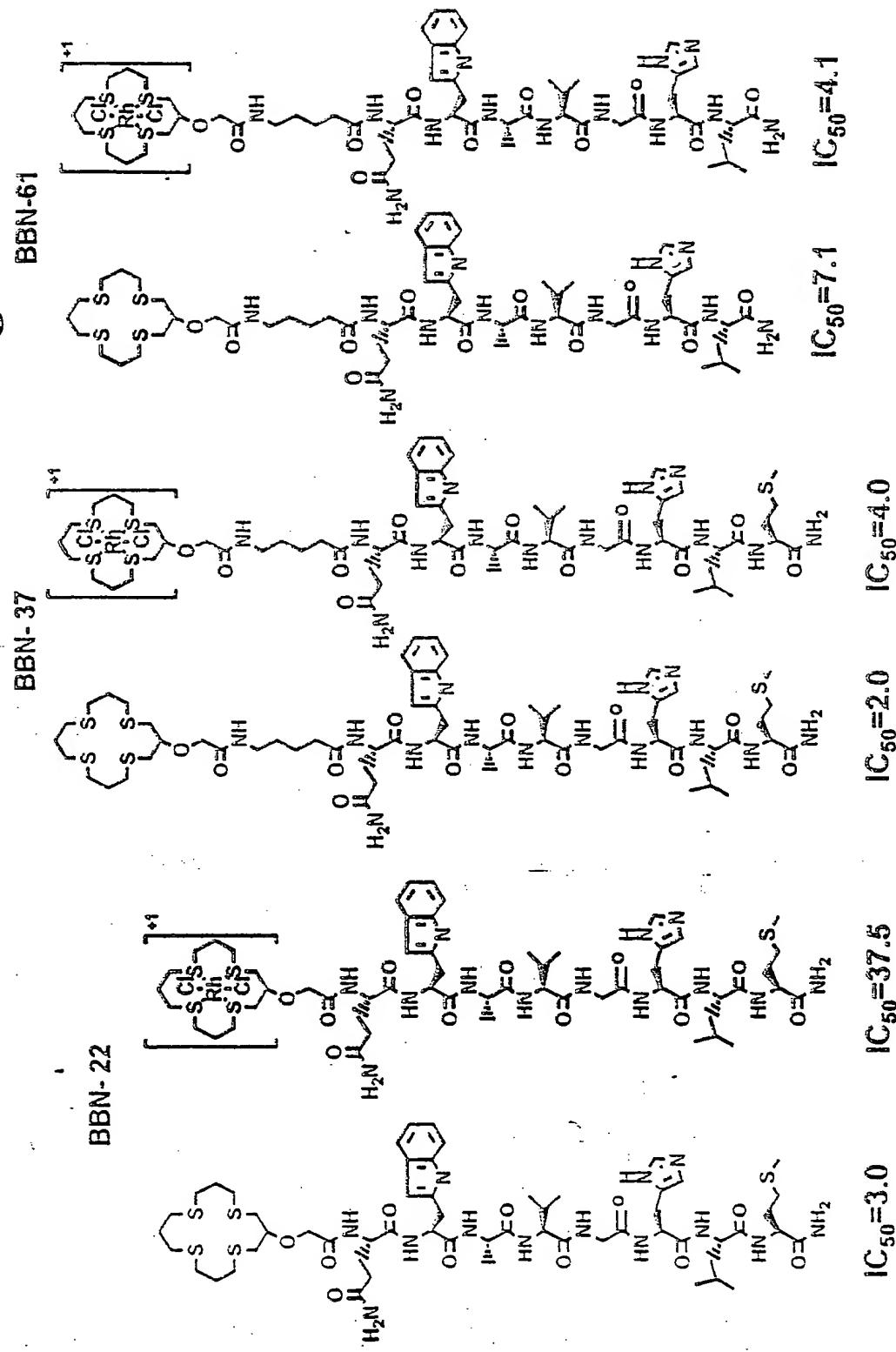


Figure 14

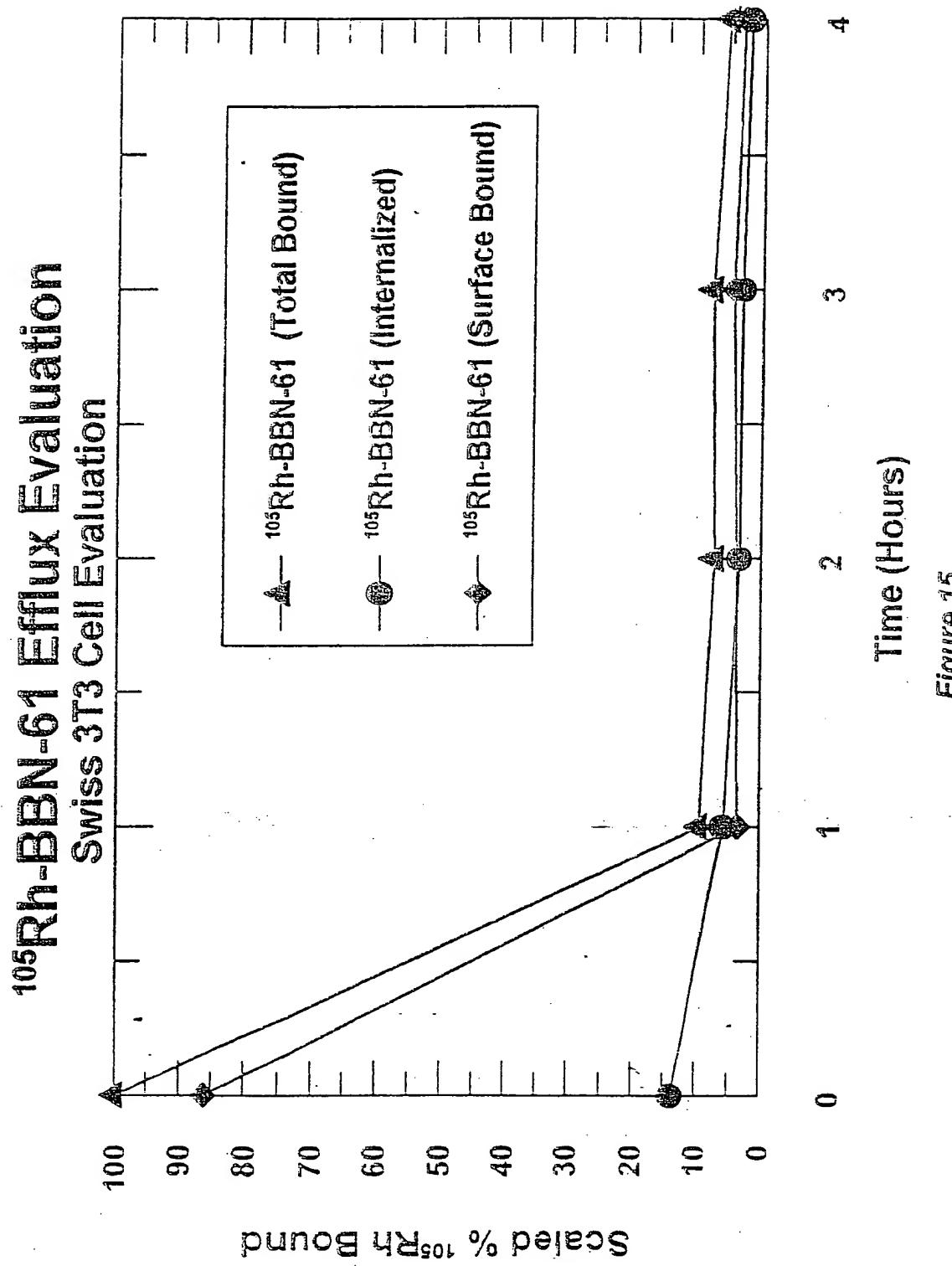


Figure 15

Efflux of ^{105}Rh -BBN-22 vs. ^{105}Rh -BBN-37 in Swiss 3T3 Cells (Non-Normalized Data)

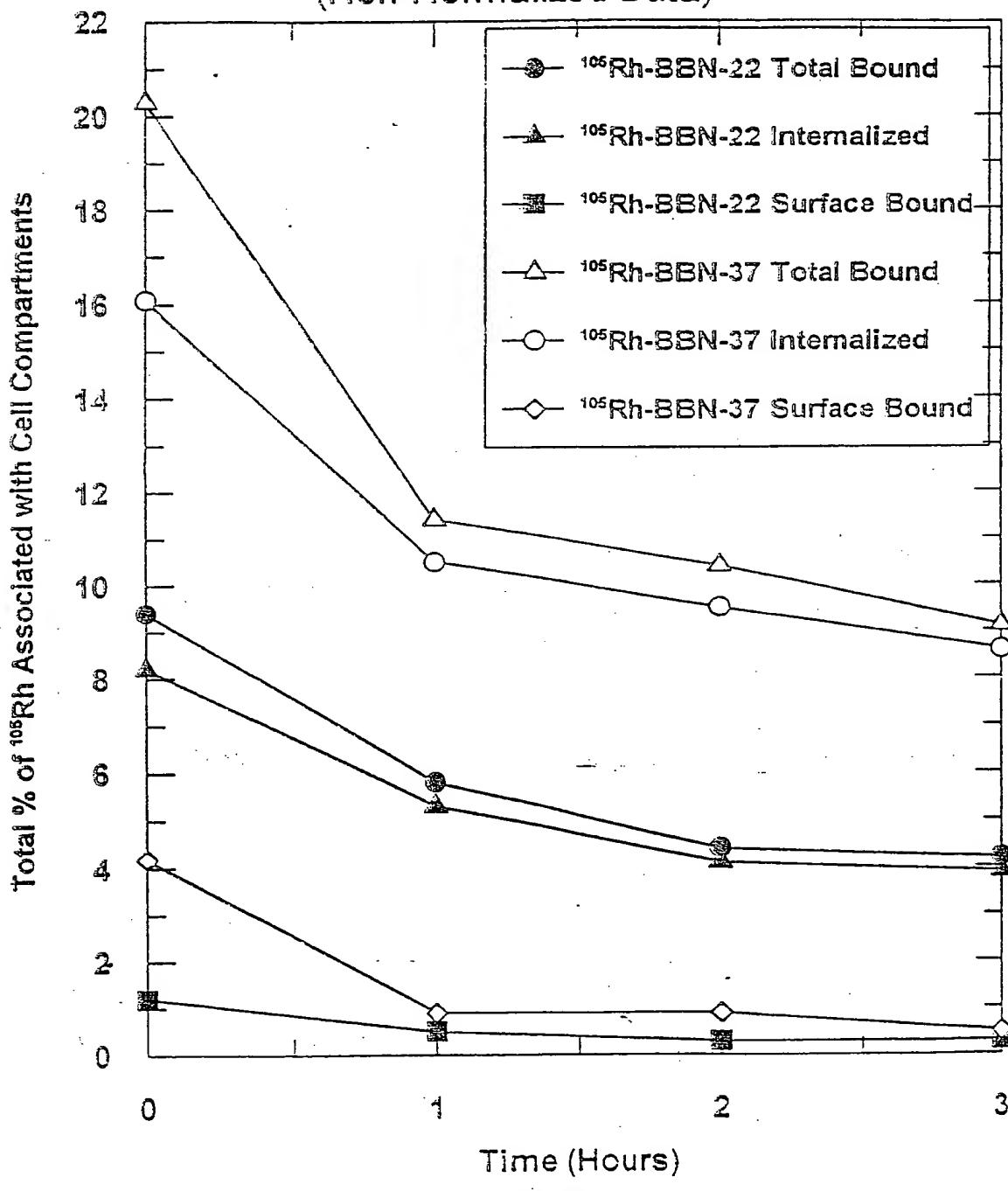
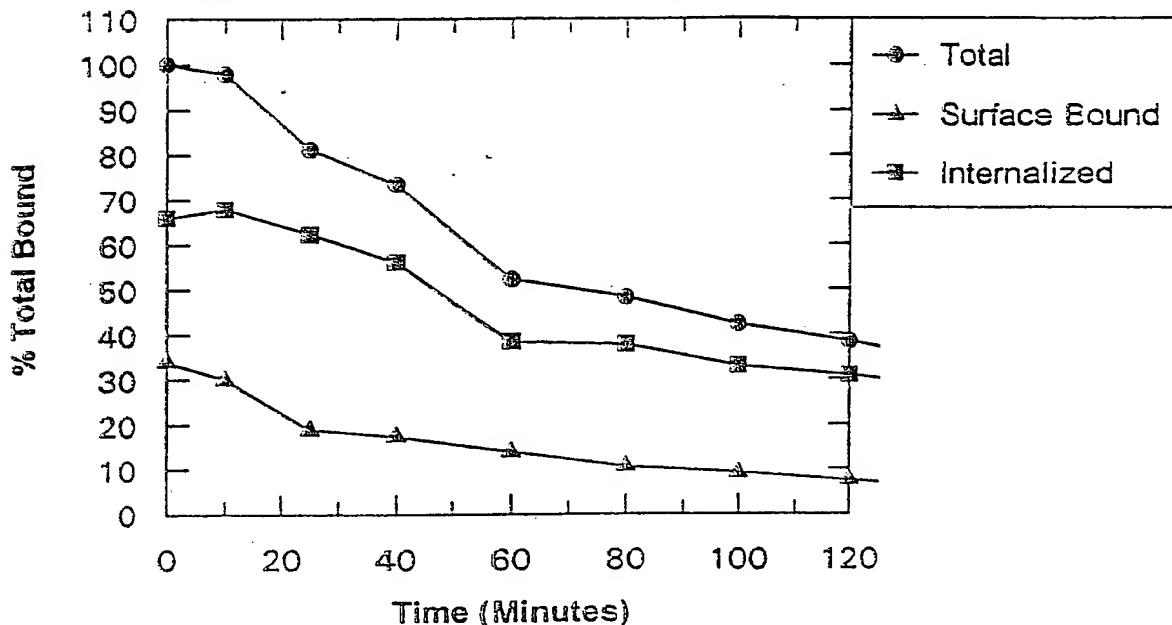


Figure 16

Pancreatic CA Cell Binding

A. Efflux of ^{125}I -Tyr⁻BBN from CF PAC1 Cells



B. Efflux of ^{105}Rh -BBN-37 from CF PAC1 Cells

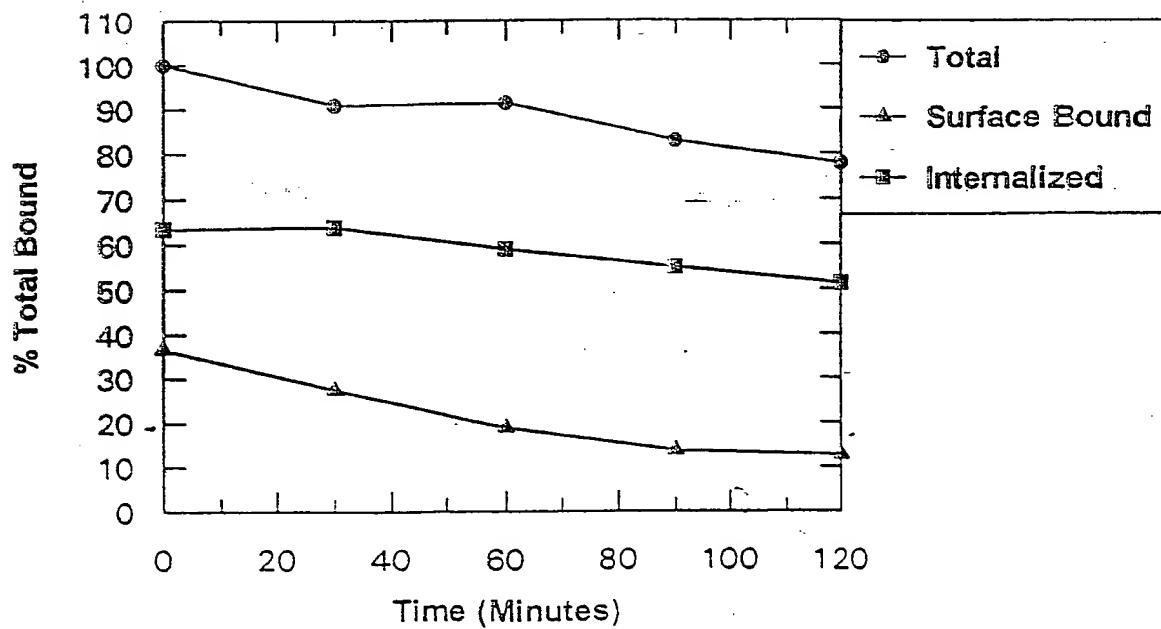
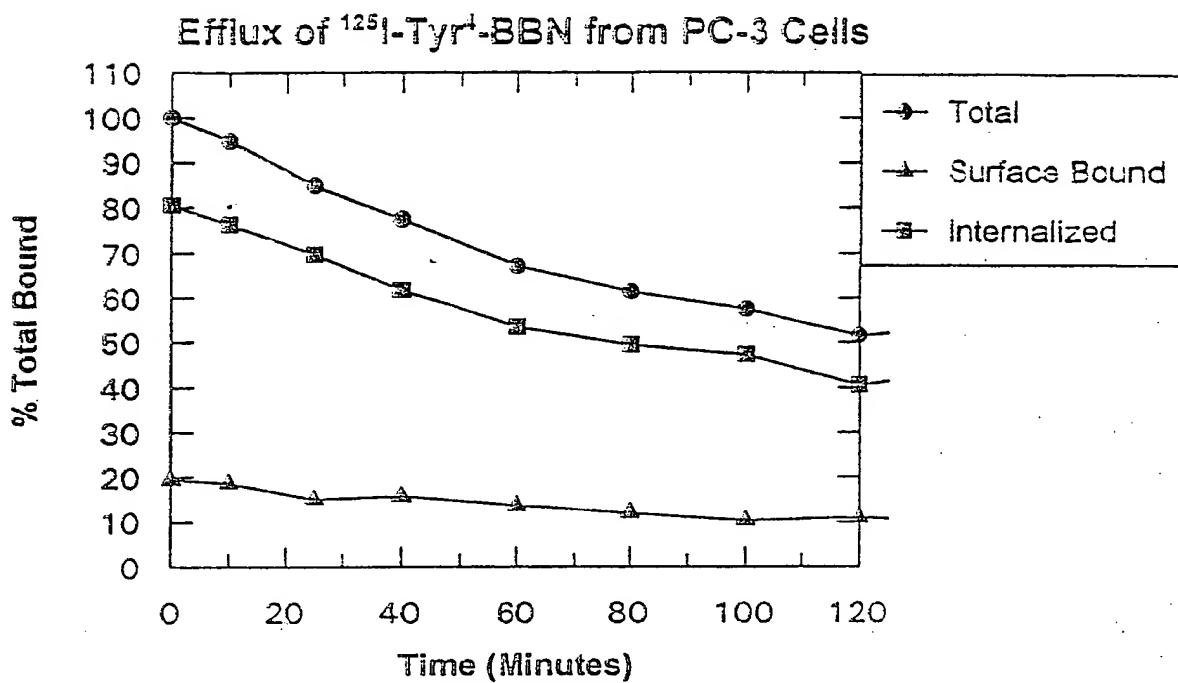


Figure 17.

Prostate CA Cell Binding

A.



B.

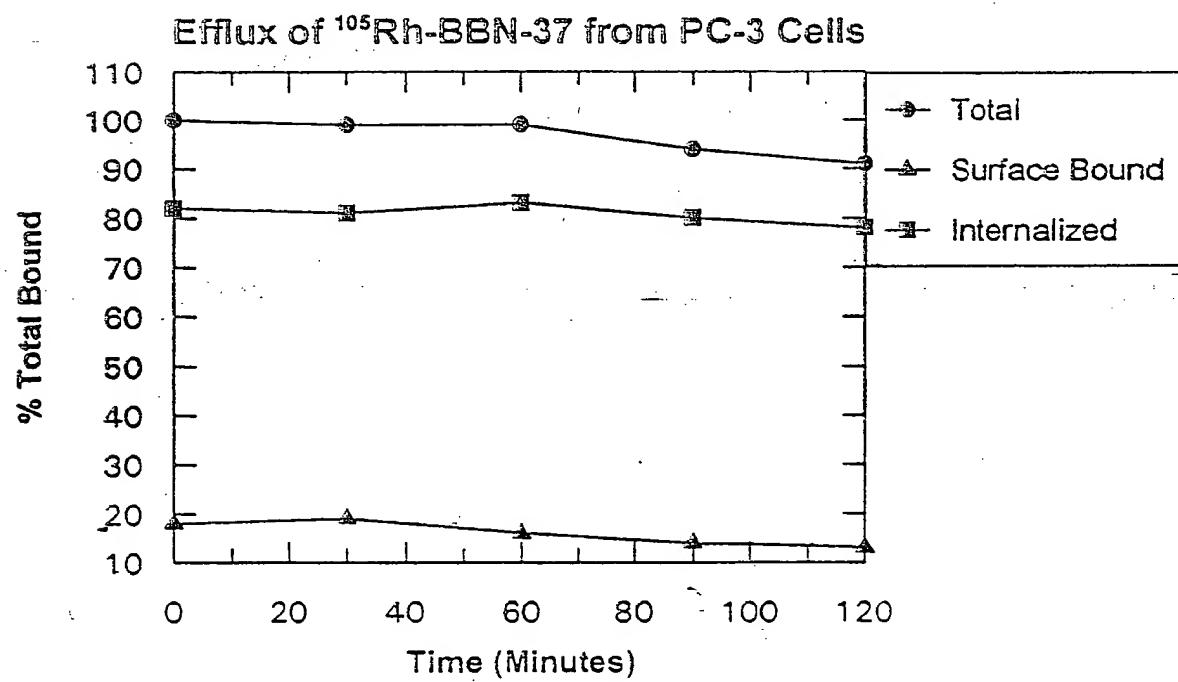


Figure 18

[16]aneS₄ Bombyxin Analogues

BBN-101

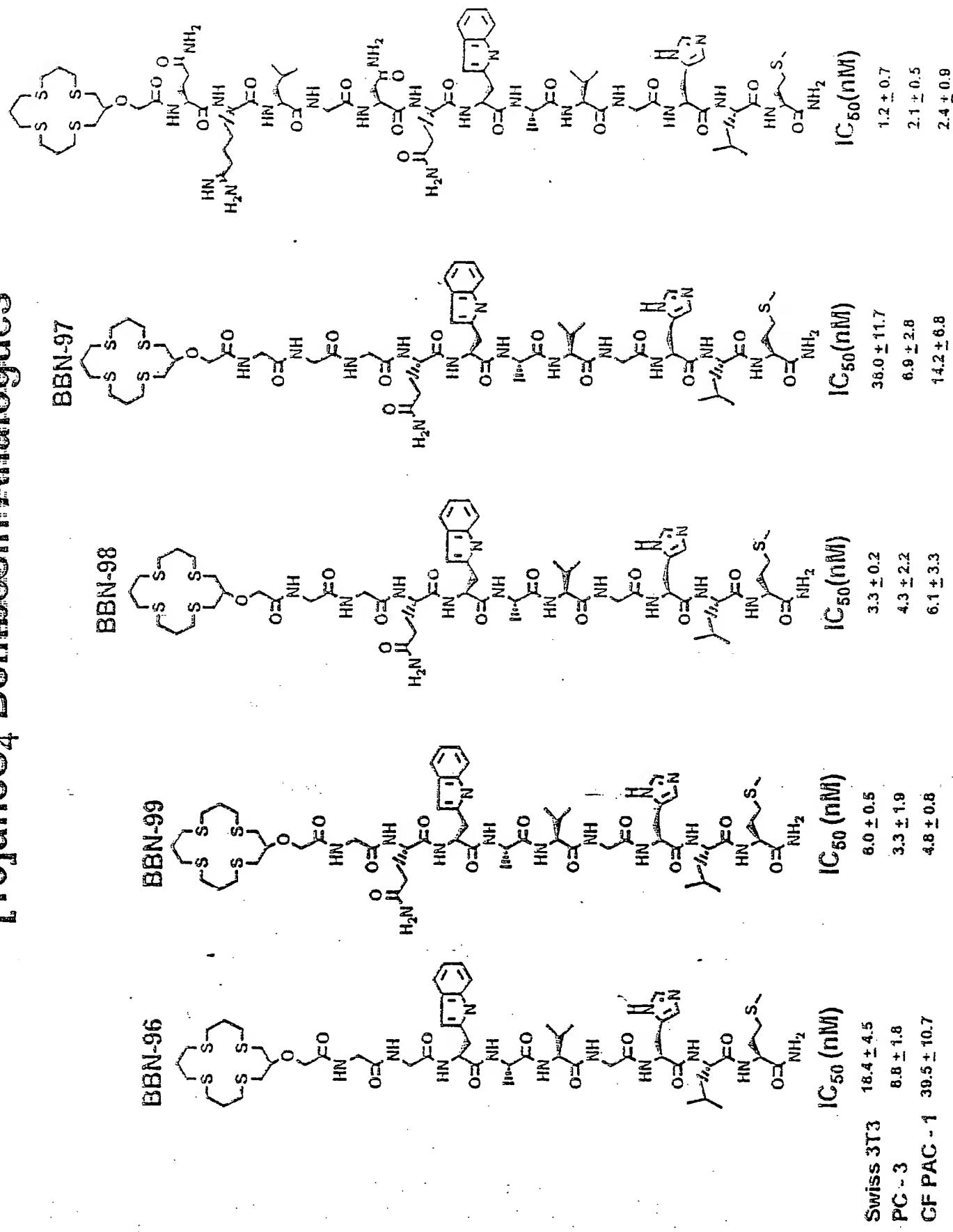
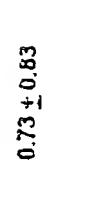
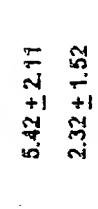
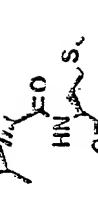
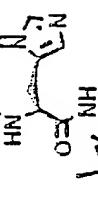
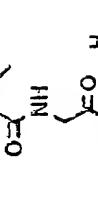
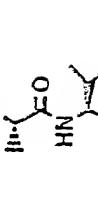
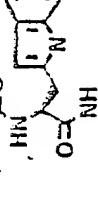
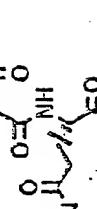
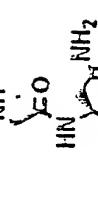
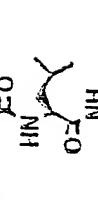
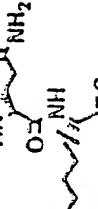
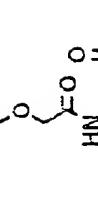
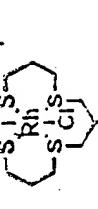


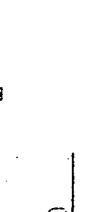
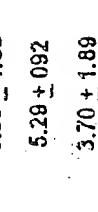
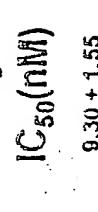
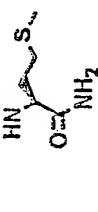
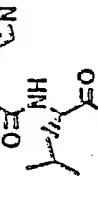
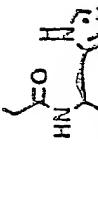
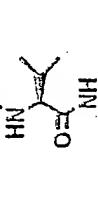
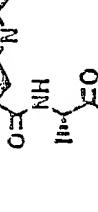
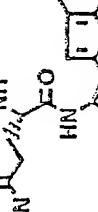
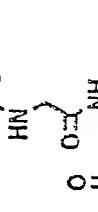
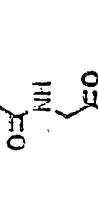
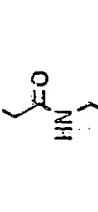
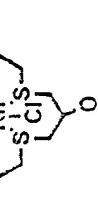
FIGURE 19

Rhodium-[16]aneS₄ Bombesin Analogues

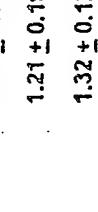
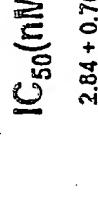
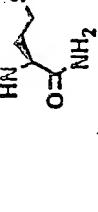
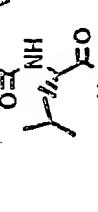
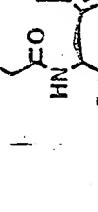
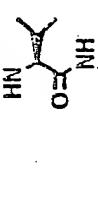
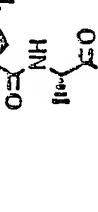
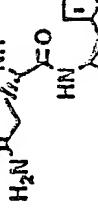
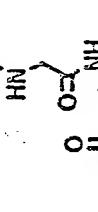
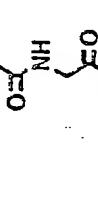
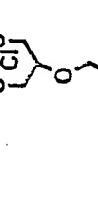
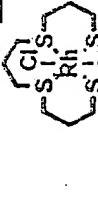
BBN-101



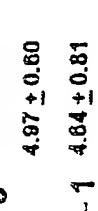
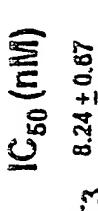
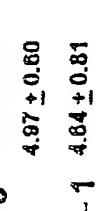
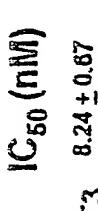
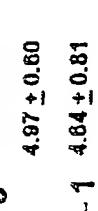
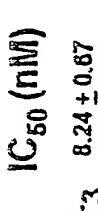
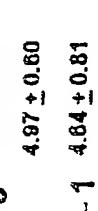
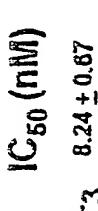
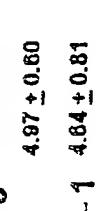
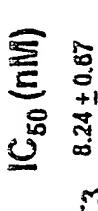
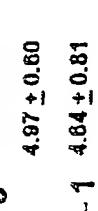
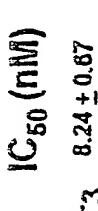
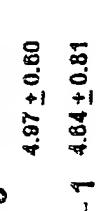
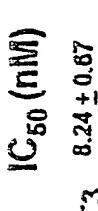
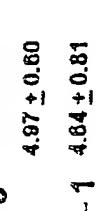
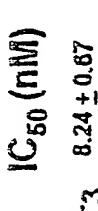
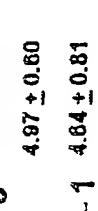
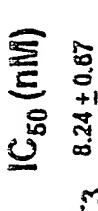
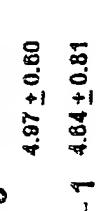
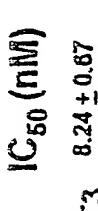
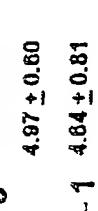
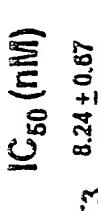
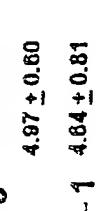
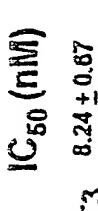
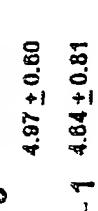
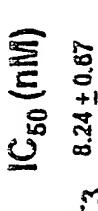
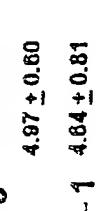
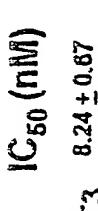
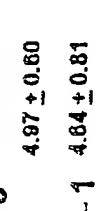
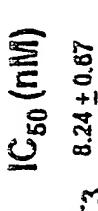
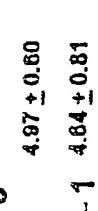
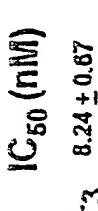
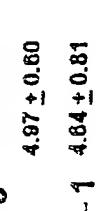
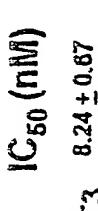
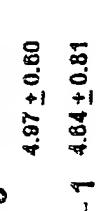
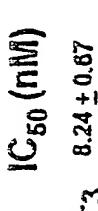
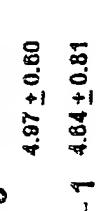
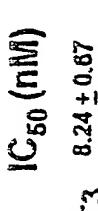
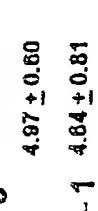
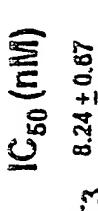
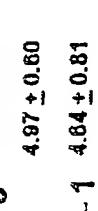
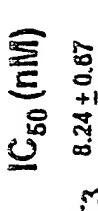
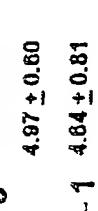
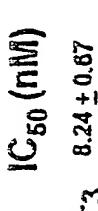
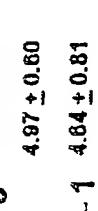
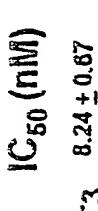
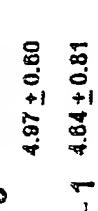
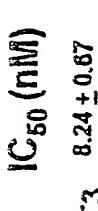
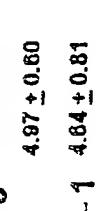
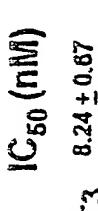
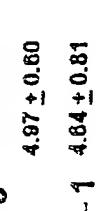
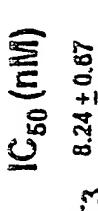
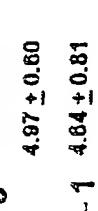
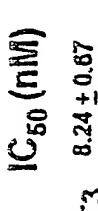
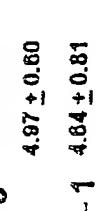
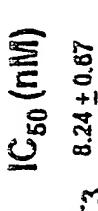
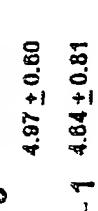
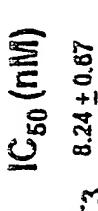
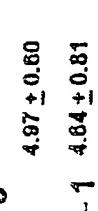
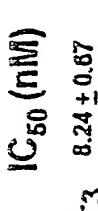
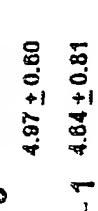
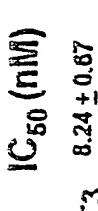
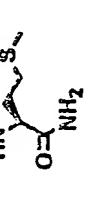
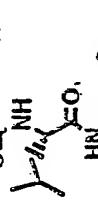
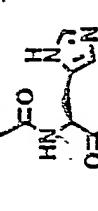
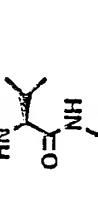
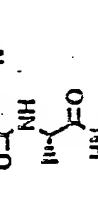
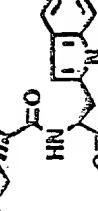
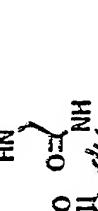
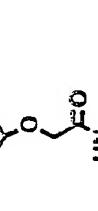
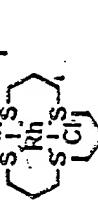
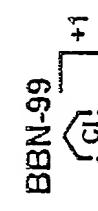
BBN-97



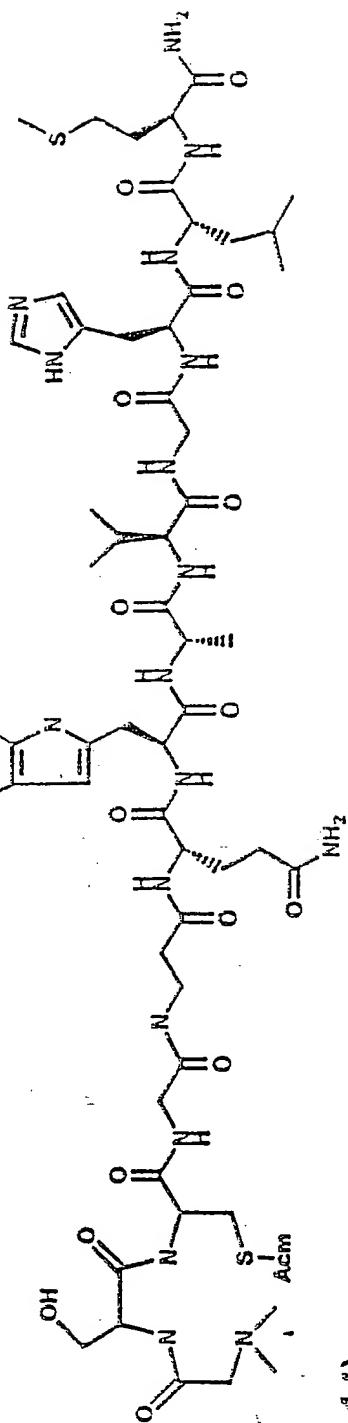
BBN-98



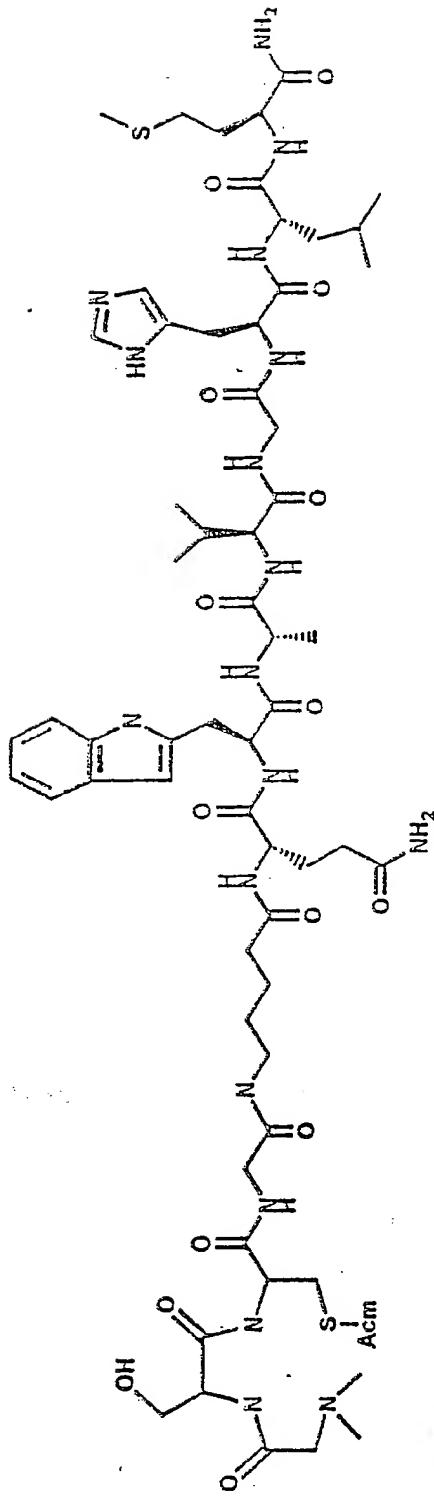
BBN-99



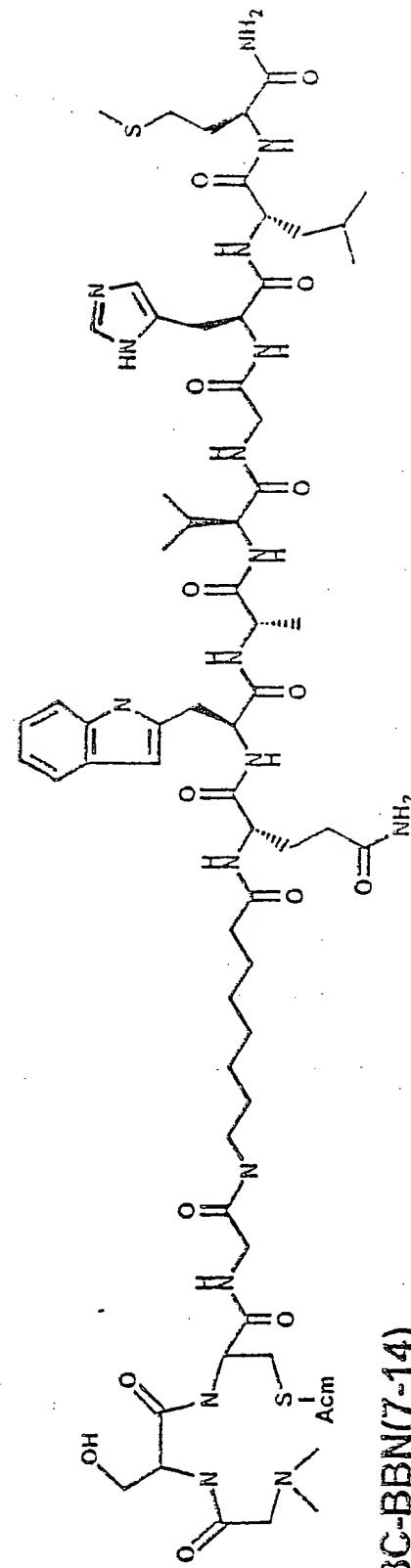
RP414-3C-BBN(7-14)



RP414-3C-BBN(7-14)



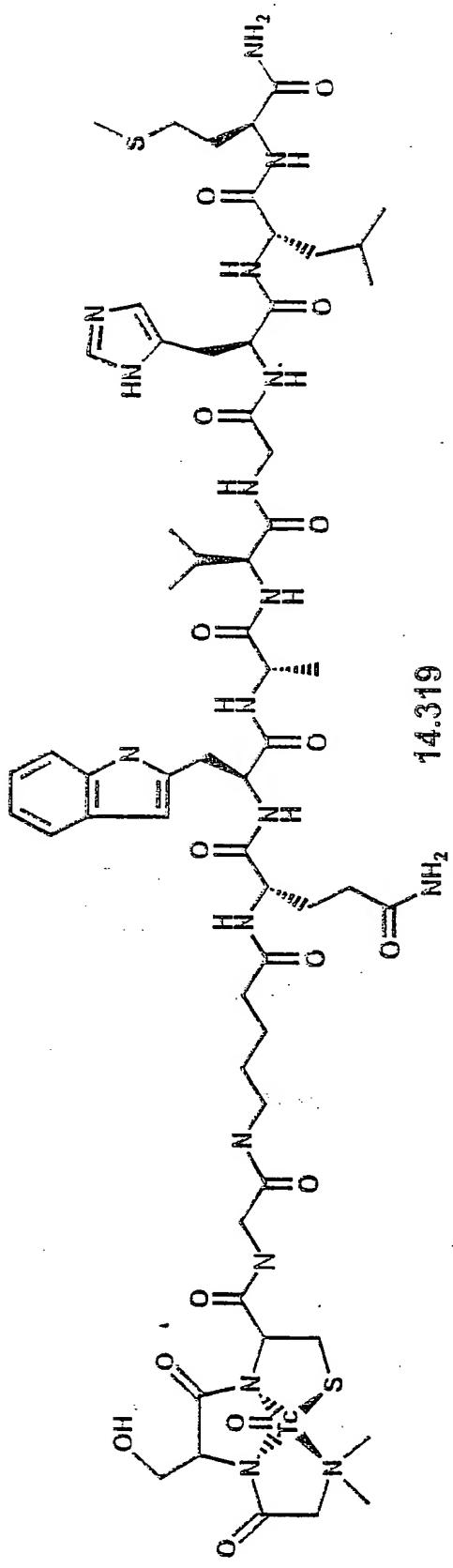
RP414-5C-BBN(7-14)



RP414-8C-BBN(7-14)

FIGURE 21

$^{99m}\text{Tc-BBN-122}$



HPLC Gradient Elution Program

Flow 1.5 ml/min
Solvent A = H_2O with 0.1% TFA
Solvent B = CH_3CN with 0.1% TFA

time(min)	%A/%B
0	95/5
25	30/70
30	95/5

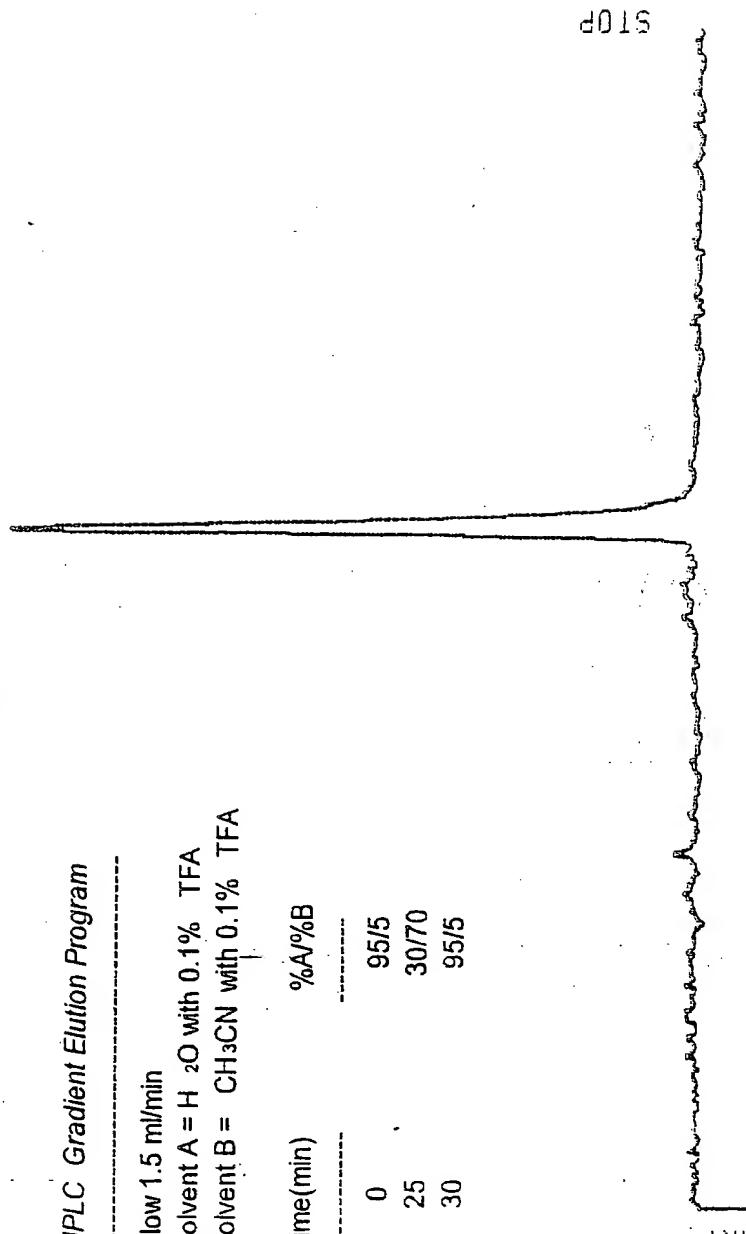


Figure 22

^{99m}Tc-BBN-122 Uptake
in Human Prostate Cancer Cells

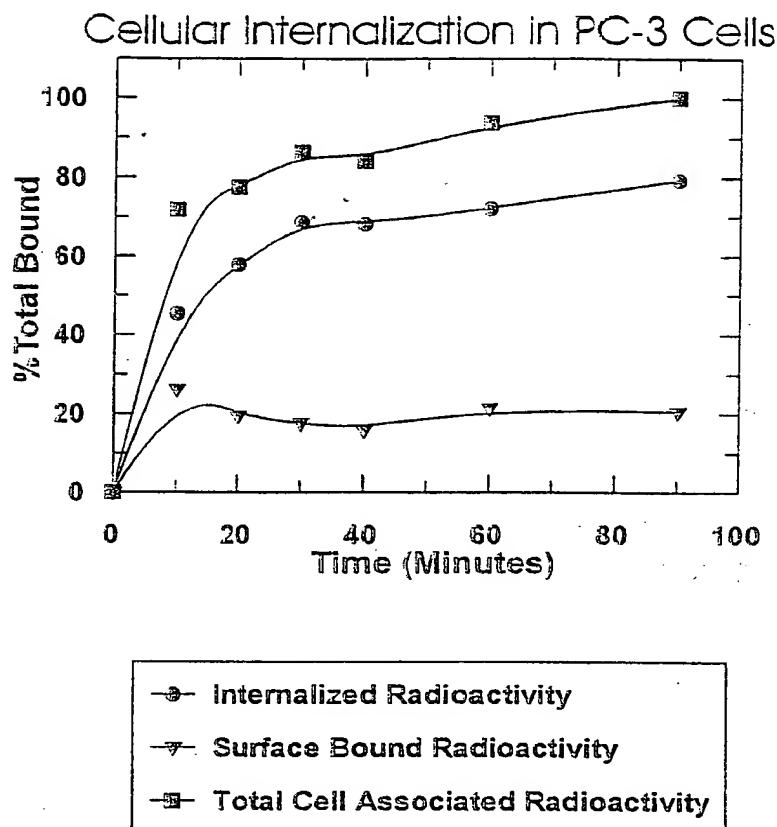


Figure 23

^{99m}Tc-BBN-122 Internalization in Human Pancreatic Cancer Cells

Cellular Internalization in CFPAC-1 Cells

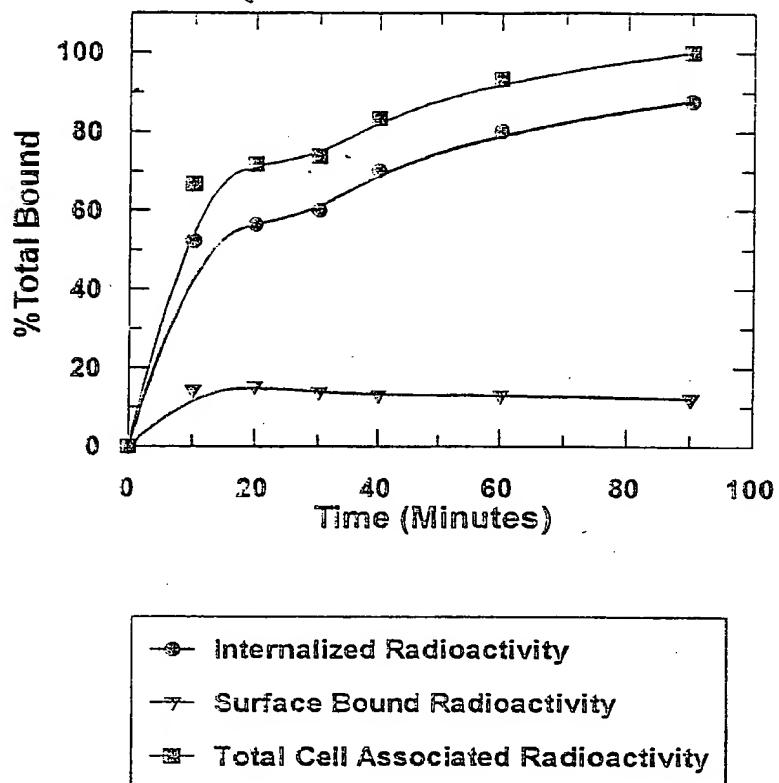


Figure 24

^{99m}Tc-BBN-122 Retention
in Human Prostate Cancer Cells

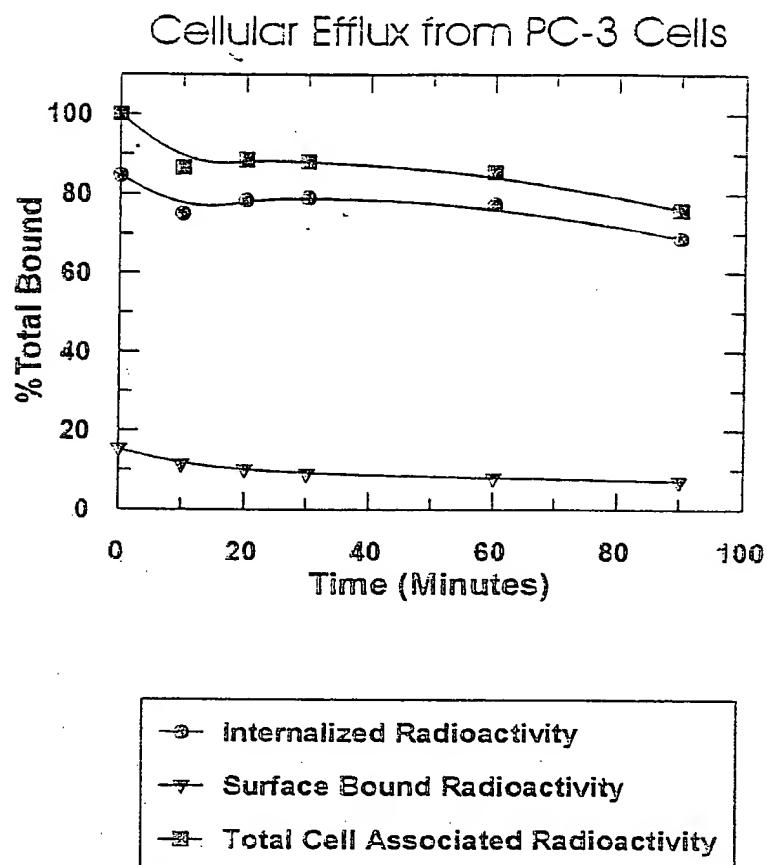


Figure 25

^{99m}Tc-BBN-122 Retention
in Human Pancreatic Cancer Cells

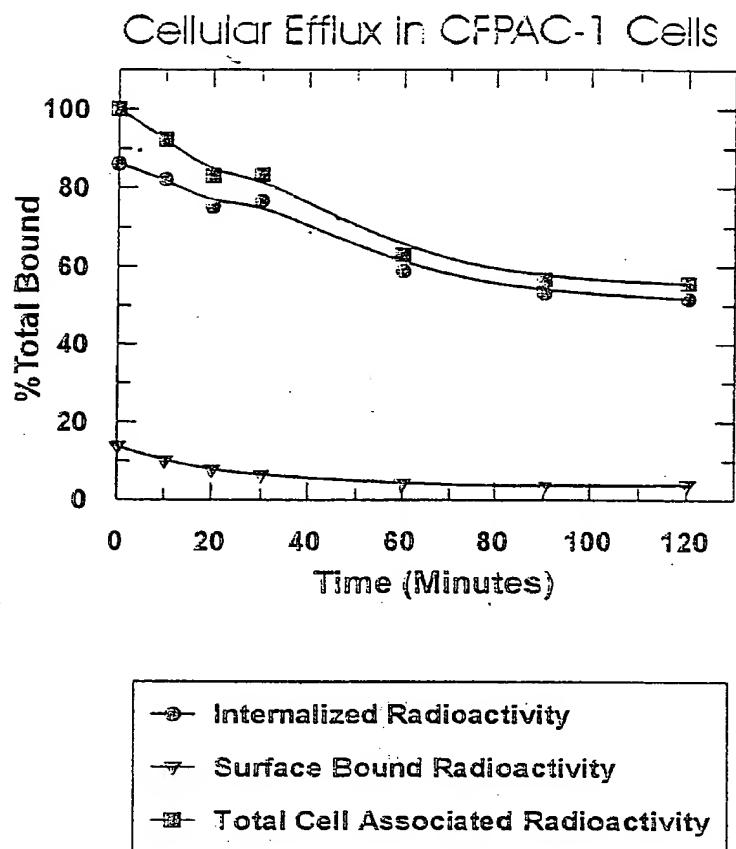
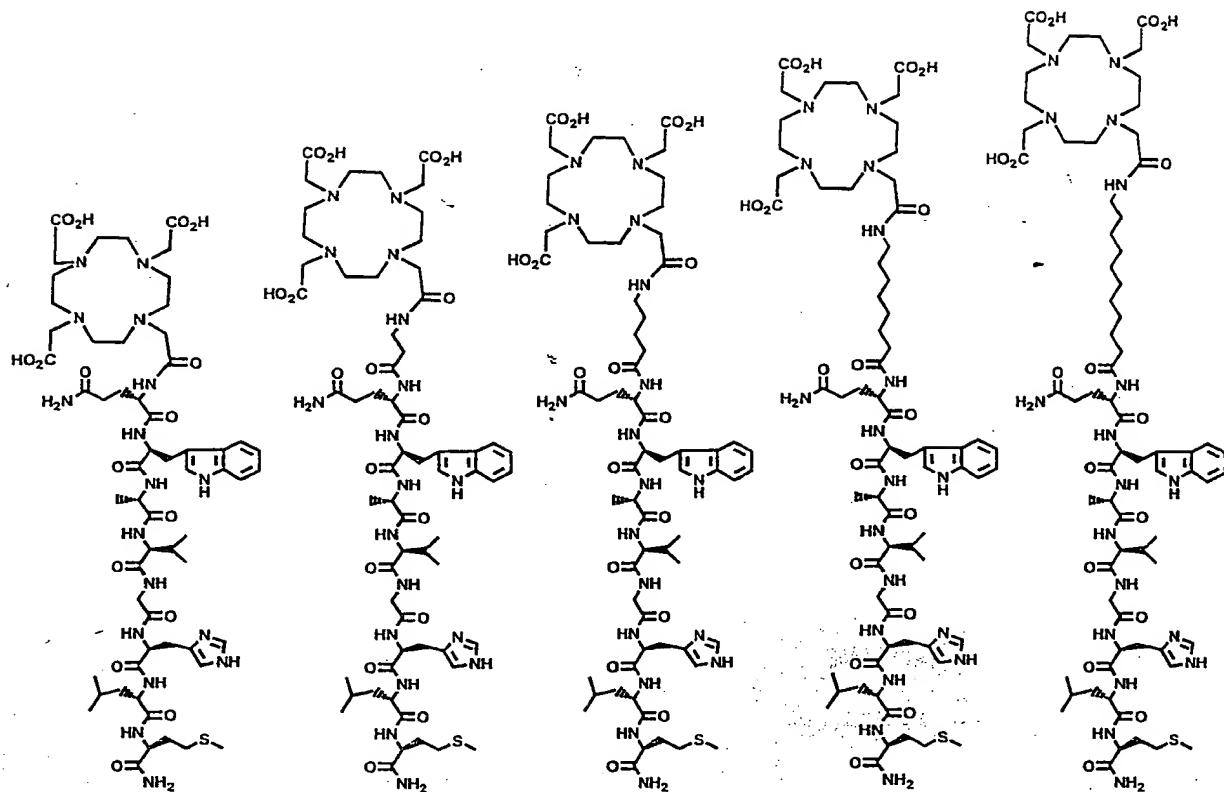


Figure 26

DOTA-BBN[7-14]NH₂ analogues.



DOTA-0-BBN(7-14)NH₂

DOTA- β Ala-BBN(7-14)NH₂ DOTA-5Ava-BBN(7-14)NH₂ DOTA-8Aoc-BBN(7-14)NH₂ DOTA-11Aun-BBN(7-14)NH₂

FIGURE 27

HPLC chromatograms of (a) DOTA-BBN[7-14]NH₂ ($\lambda = 280$ nm) (b) In-DOTA-BBN[7-14]NH₂ ($\lambda = 280$ nm) and (c) ¹¹¹In-DOTA-BBN[7-14]NH₂ (radiometric).

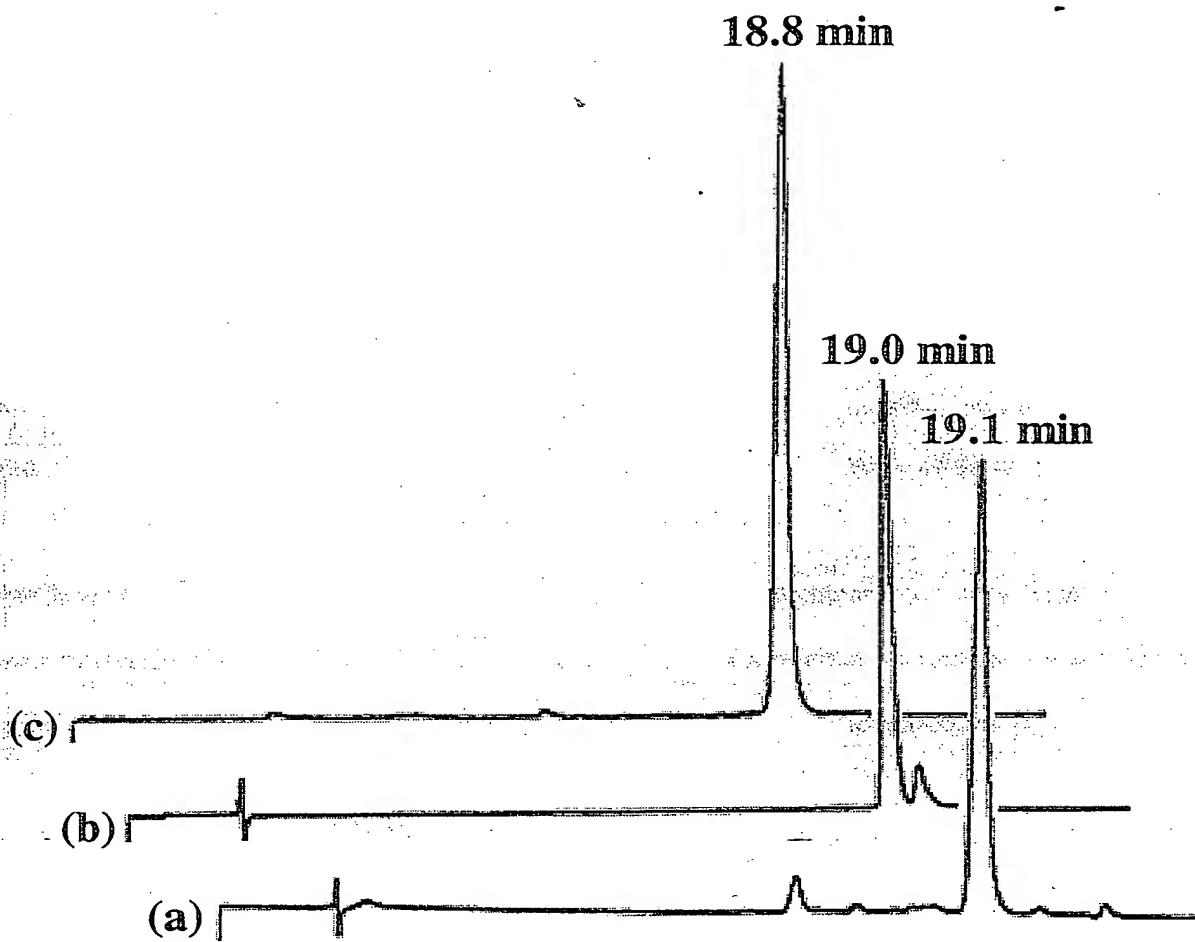


FIGURE 28

Competitive binding assay of In-DOTA-8-Aoc-BBN[7-14]NH₂ vs. ¹²⁵I-Tyr⁴-BBN in PC-3 cells.

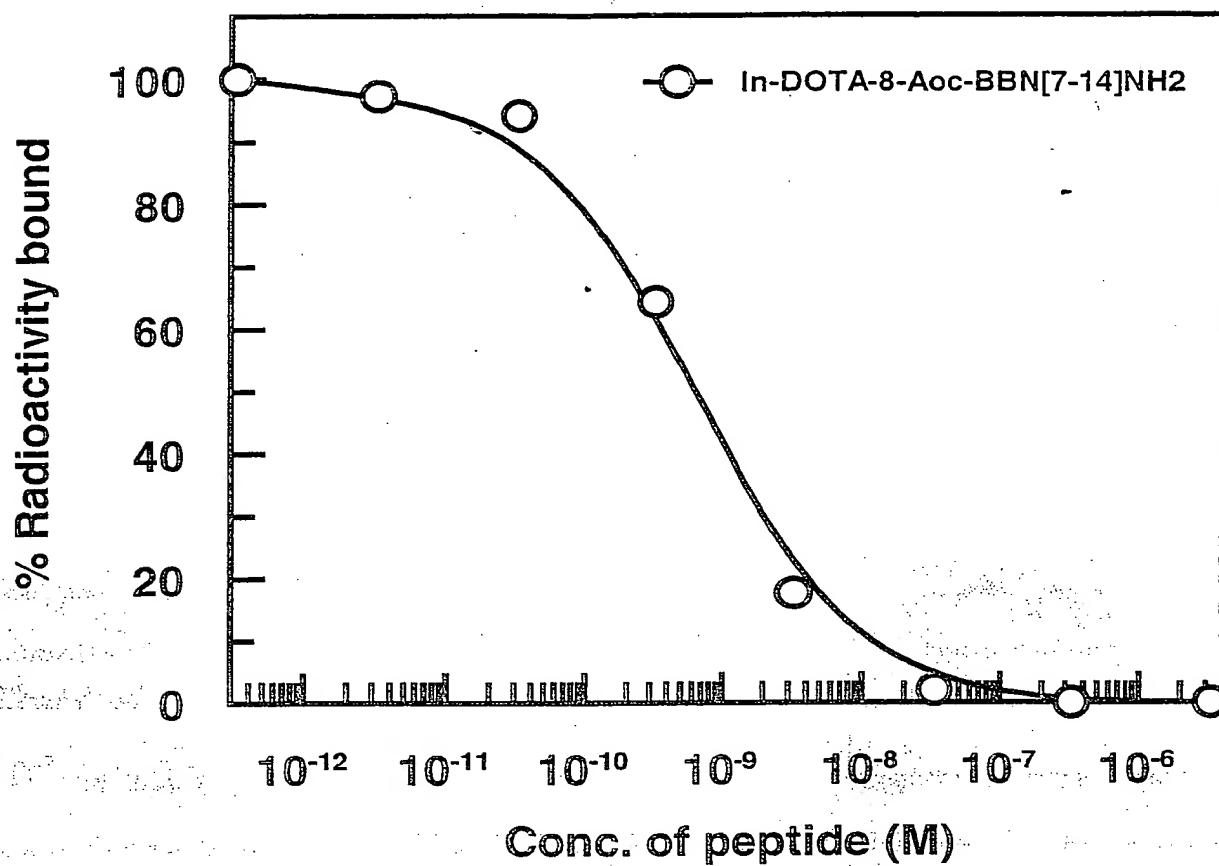


FIGURE 29

Internalization of ^{111}In -DOTA-8-Aoc-BBN[7-14] NH_2 in PC-3 cells.

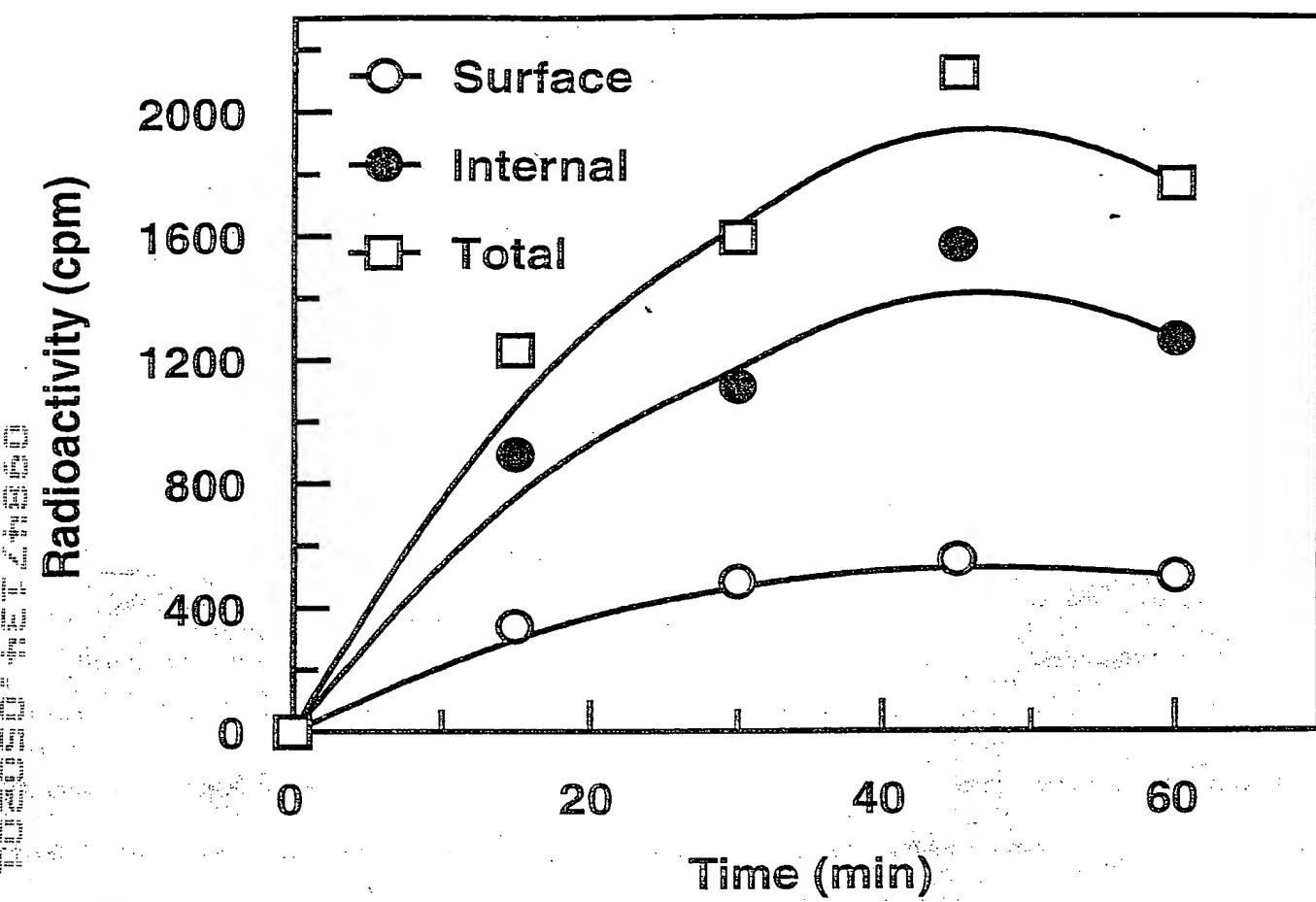


FIGURE 30

Efflux of ^{111}In -DOTA-8-Aoc-BBN[7-14] NH_2 in PC-3 cells.

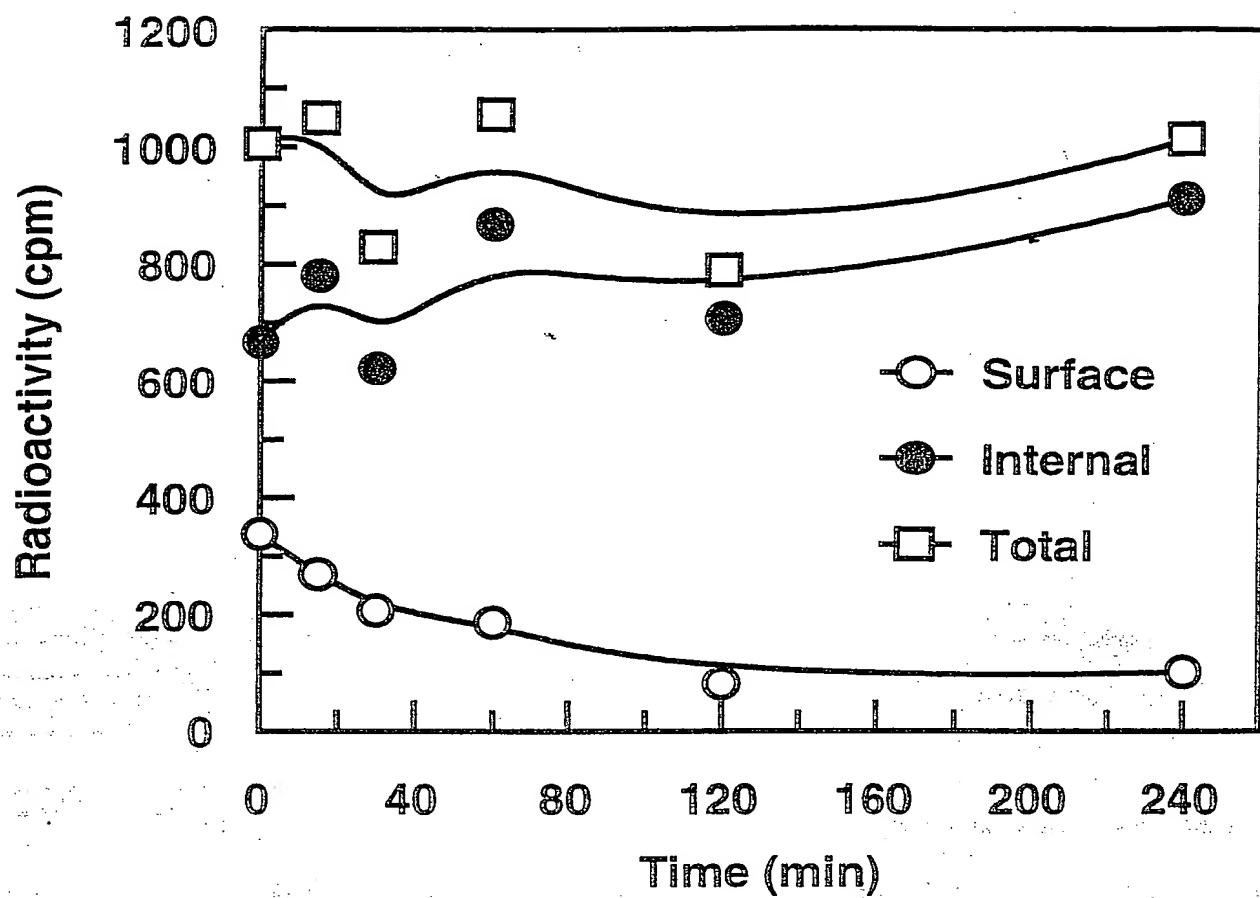


FIGURE 31

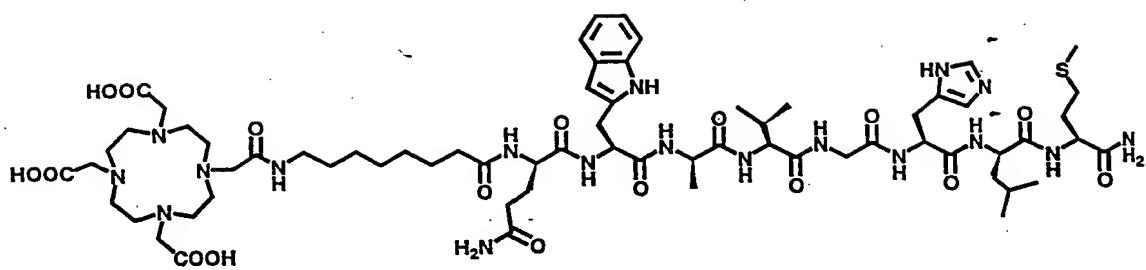


Figure 32